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Cognitive Rehabilitation on Chemotherapy-Related Cognitive Impairments: A Systematic Review

Reabilitação Cognitiva nos Défices Cognitivos Relacionados à Quimioterapia: Uma Revisão Sistemática

Rehabilitación cognitiva en los déficits cognitivos relacionados con la quimioterapia: Una revisión sistemática

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Abstract

Cancer is a major public health issue. Although chemotherapy is effective in treating cancer, it is associated with various cognitive deficits. This study aimed to review neuropsychological and cognitive rehabilitation along with intervention protocols for patients experiencing cognitive alterations due to chemotherapy. This systematic review followed the PRISMA 2020 guidelines. PubMed, Bireme (Virtual Health Library, BVS), and Cochrane Library were used as databases. The search identified 327 articles. After screening, 15 were selected for full-text review, of which six met the eligibility criteria. Thus, the final sample included six studies. The study highlights the heterogeneity of neuropsychological assessment protocols, limiting result comparisons. Further research is needed to assess existing interventions and standardize evaluation protocols.

Keywords: Chemotherapy-Related Cognitive Impairment, Cognitive Training, Rehabilitation, Neuropsychological Tests, Cognitive Behavior Therapy

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Resumo

O câncer é um grande problema de saúde pública. Embora a quimioterapia seja eficaz no seu tratamento, ela está associada a déficits cognitivos. Este estudo teve como objetivo revisar os protocolos de reabilitação neuropsicológica e cognitiva e as intervenções para pacientes com alterações cognitivas devido à quimioterapia. Esta revisão sistemática seguiu as diretrizes PRISMA 2020. Foram utilizadas como bases de dados o PubMed, Bireme (Biblioteca Virtual em Saúde - BVS) e Cochrane Library. A busca identificou 327 artigos. Após a triagem, 15 foram selecionados para revisão completa do texto, dos quais seis atenderam aos critérios de elegibilidade. Assim, a amostra final foi composta por seis estudos. O estudo destaca a heterogeneidade dos protocolos de avaliação neuropsicológica, limitando a comparação dos resultados. Mais pesquisas são necessárias para avaliar as intervenções existentes e padronizar os protocolos de avaliação.

Palavras-chave: Déficit Cognitivo Relacionado à Quimioterapia, Treinamento Cognitivo, Reabilitação, Testes Neuropsicológicos, Terapia Cognitivo-Comportamental

Resumen

El cáncer es un gran problema de salud pública. Aunque la quimioterapia es eficaz en su tratamiento, está asociada con déficits cognitivos. Este estudio tuvo como objetivo revisar los protocolos de rehabilitación neuropsicológica y cognitiva, así como las intervenciones, para pacientes con alteraciones cognitivas debido a la quimioterapia. Esta revisión sistemática siguió las directrices PRISMA 2020. Se utilizaron como bases de datos PubMed, Bireme (Biblioteca Virtual en Salud - BVS) y Cochrane Library. La búsqueda identificó 327 artículos. Tras la selección, 15 fueron elegidos para revisión completa del texto, de los cuales seis cumplieron los criterios de elegibilidad. Así, la muestra final estuvo compuesta por seis estudios. El estudio destaca la heterogeneidad de los protocolos de evaluación neuropsicológica, lo que limita la comparación de los resultados. Se requiere más investigación para evaluar las intervenciones existentes y estandarizar los protocolos de evaluación.

Palabras clave: Deterioro Cognitivo Relacionado con la Quimioterapia, Entrenamiento Cognitivo, Rehabilitación, Pruebas Neuropsicológicas, Terapia Cognitivo-Conductual

Highlights of Clinical Impact

- Patients reported deficits that significantly differed from the results of formal tests, making identification and intervention more challenging.
- Neuropsychological rehabilitation programs improved cognition and helped reduce anxiety and depression levels.
- Researchers use varied protocols, with measures and assessments also differing across studies, making standardization challenging.

Cancer is one of the main public health problems in the world. With advances in treatment, the number of survivors grew 69.2 % between the years 2014–2020 (National Cancer Institute, 2024). Besides that, it is estimated that the incidence of new cases around the year 2040 will reach 19.9M individuals between 20 and 74 years of age, with 9.60M deaths (World Health Organization, 2020). Cancer treatments and interventions (e.g., surgery, chemotherapy, and radiotherapy) may result in a decrease in an individual's social, occupational, and cognitive functioning (National Cancer Institute, 2024). Furthermore, limitations arising from the disease itself can cause significant emotional distress, including a reduction in the quality of life of those affected by this condition (Campos et al., 2021; Hodgson et al., 2013; Oliveira et al., 2023).

Despite the efficacy of chemotherapy in cancer treatment, studies have demonstrated that this therapeutic approach can lead to several cognitive deficits (Anderson-Hanley et al., 2003; de Ruiter et al., 2011; Fernandes et al., 2019; Stewart et al., 2006; Tong et al., 2020). The mechanisms responsible for these deficits remain uncertain (Mounier, et al. 2020), but several studies have attempted to elucidate the etiological mechanisms of the potential cognitive impairments derived from chemotherapy, based on at least three main hypotheses: 1) genetic predisposition; 2) consequence of treatment and dosage, particularly chemotherapy treatment which can lead to neurotoxicity; and 3) individual factors associated with the process of diagnosis and treatment of cancer, such as pre-existing or developed anxiety, stress, and depression, as a result of the aforementioned social impacts (Bai & Yu, 2021). There is a significant discrepancy between the results based on self-reports of cognitive deficits when compared to the results of formal tests, thus complicating the identification of this condition and subsequent intervention processes (Craig et al. 2014; Wefel et al., 2011).

Based on current literature, pharmacotherapy (Berridge et al., 2011; Iarkov et al., 2016; Winocur et al., 2011; Yang & Von Ah, 2024), cognitive-behavior psychotherapy (Ferguson et al.,

2012; Zhang et al, 2020), and cognitive rehabilitation are used to help patients with cognitive deficits. Despite the effectiveness of the aforementioned procedures, this paper will focus on cognitive rehabilitation.

COGNITIVE REHABILITATION AND CHEMOTHERAPY

Cognitive rehabilitation includes the training of cognitive skills that may have been impaired by illness or specific treatments (Országhová, Mego, & Chovanec, 2021; Von Ah & Crouch, 2020). This approach has yielded positive outcomes in the context of brain injury programs for mild cognitive impairment in the elderly, multiple sclerosis, schizophrenia, and brain tumor patients (Cherrier et al., 2013; Klaver et al., 2024).

According to Ahles and Root (2018), managing cognitive deficits involves instructing patients to regulate their pace during cognitive activities to address cognitive fatigue, minimize distractions, plan and organize time, and utilize calendars, day planners, and mnemonic strategies. Furthermore, a crucial component of cognitive rehabilitation is education regarding brain function, cognitive deficits, and their implications for daily activities.

Two primary approaches to rehabilitation can be identified: computer-based and strategy training. Computer-based training involves the retraining of cognitive skills through practice utilizing computerized tasks. Strategy training, conversely, is a behavior-oriented program that aims to retrain lost cognitive skills and compensatory strategies, it may also incorporate psychoeducation, stress reduction, or peer support (Collins et al., 2013; Pedras et al., 2022). Several forms of rehabilitation are currently being evaluated for cognitive rehabilitation in patients with chemotherapy-induced cognitive impairment, such as the application of psychoeducation techniques and computer-assisted rehabilitation, through software programs including Insight RehaCo, Happy Neuron, and Cogmed (Binarelli et al., 2021; Bray et al., 2017; Liang et al., 2019; Myers et al., 2020).

A rehabilitation model that has gained prominence and is closely related to cognitive and behavioral therapies is the holistic model of rehabilitation, an approach that aims to address not only cognitive functions but also promote improvements in the metacognitive, interpersonal, functional, and emotional aspects of each patient (Cicerone et al., 2008). To achieve this, rehabilitation programs involve interventions that encourage the individual's understanding, awareness, and acceptance of their situation, as well as the development of compensatory skills to minimize the impact of such difficulties (Wilson, 2008). These strategies may include individual and/or group therapies (Skurlova et al., 2024; Untura & Rezende, 2012; Van Heugten & Wilson, 2021; Wilson, 2008).

Holistic neuropsychological rehabilitation is grounded in a perspective that recognizes that rehabilitative processes must include cognitive-behavioral interventions aimed at improving performance in cognitive and functional domains, while also addressing social, emotional, and functional issues related to the individual's disability, injury, or condition. In other words, holistic approaches to neuropsychological rehabilitation require efforts in both cognitive rehabilitation and psychotherapy, with the goal of helping individuals achieve optimal psychosocial adjustment (Wilson, 2008). In this context, our research aimed to investigate which rehabilitation and intervention protocols are being employed in patients with cognitive deficits resulting from chemotherapy, assess which cognitive functions have been addressed more frequently, and identify the outcomes achieved through these clinical practices.

METHOD

Study Design

This study adheres to the PRISMA 2020 guidelines for systematic reviews. We used PubMed, Bireme (Virtual Health Library – BVS), and the Cochrane Library as our primary databases, covering a research period from February 2022 to December 2024. These databases were selected for their extensive range of English-language articles and their comprehensive coverage of diverse study types and methodologies, including clinical trials and systematic reviews. This selection ensured the inclusion of recent and relevant information. The study is registered in PROSPERO under registration number CRD42022299277 [omitted for review purposes]. Our search terms and strategy included: ("cognitive rehabilitation" OR "neuropsychological rehabilitation") AND (Chemotherapy OR Antineoplastic OR chemobrain) AND ("executive function" OR memory OR attention OR cognition OR "cognitive function" OR "cognitive functions" OR "executive functions").

Inclusion and Exclusion Criteria

PICO strategy: Our study employed the Patient, Intervention, Control, and Outcomes (PICO) strategy to develop hypotheses, select, and analyze articles (see Table 1).

Table 1. Results of the risk of bias assessment using RoB2.

Acronym	Definition	Description
P	Population/Patient	Patients with cognitive impairments resulting from chemotherapy treatment
I	Intervention	Use of cognitive/neuropsychological rehabilitation in patients who underwent cancer treatment
C	Comparison	Not specified, as the research did not include a comparison group
O	Outcome	Improvements in the quality of life and functions of the patients after the intervention

Inclusion criteria were a) articles published in English; b) studies describing cognitive or neuropsychological rehabilitation in adult and elderly patients; and c) research on cognitive rehabilitation for chemotherapy-induced cognitive impairment from any cancer type. Exclusion criteria were a) review articles; b) articles focused solely on evaluation processes; c) studies on interventions unrelated to cognitive rehabilitation; d) studies on pediatric populations; e) articles lacking connections between rehabilitation and chemotherapy; and f) studies using rehabilitation for unrelated health issues. Year of publication was not an exclusion criterion.

Selection Method

The selection process began with an independent, blinded review of article titles and abstracts by five invited researchers. Rayyan software facilitated blinded analysis and duplicate identification, streamlining the initial screening process. The selected articles were reviewed comprehensively to confirm eligibility. During abstract analysis, data were compared against the established criteria.

Data Extraction and Quality Assessment

After the previous process, we conducted a full review of each study, extracting key information: author names, publication year, study design, participant details (number, age, gender), cognitive assessment methods, neuropsychological test results, intervention details (type, frequency), primary and secondary outcomes, adverse effects, and future directions.

Quality and risk of bias were assessed using the Revised Cochrane risk-of-bias 2 (RoB2) tool for randomized trials. This tool analyzes risk across several domains: bias from randomization, deviations from intended interventions, missing outcome data, outcome measurement, and selective outcome reporting. Low risk of bias requires all domains to be categorized as low. Among the six included studies, three were longitudinal, showing varying degrees of bias, while others (Poppelreuter et al., 2009; Vardy et al., 2023) presented an elevated presence of bias, reducing confidence in those results.

Data Synthesis

Data presentation in the current study follows a structured format. In the Results section, findings are detailed, starting with search characterization, quality assessment outcomes, participant demographics, cognitive assessments, self-report measures, and rehabilitation interventions used (see Table 2).

RESULTS

Search results

The search yielded 327 studies. Fifteen were selected for full review, and six met the study's criteria, thereby assuring their inclusion for the review (see Figure 1).

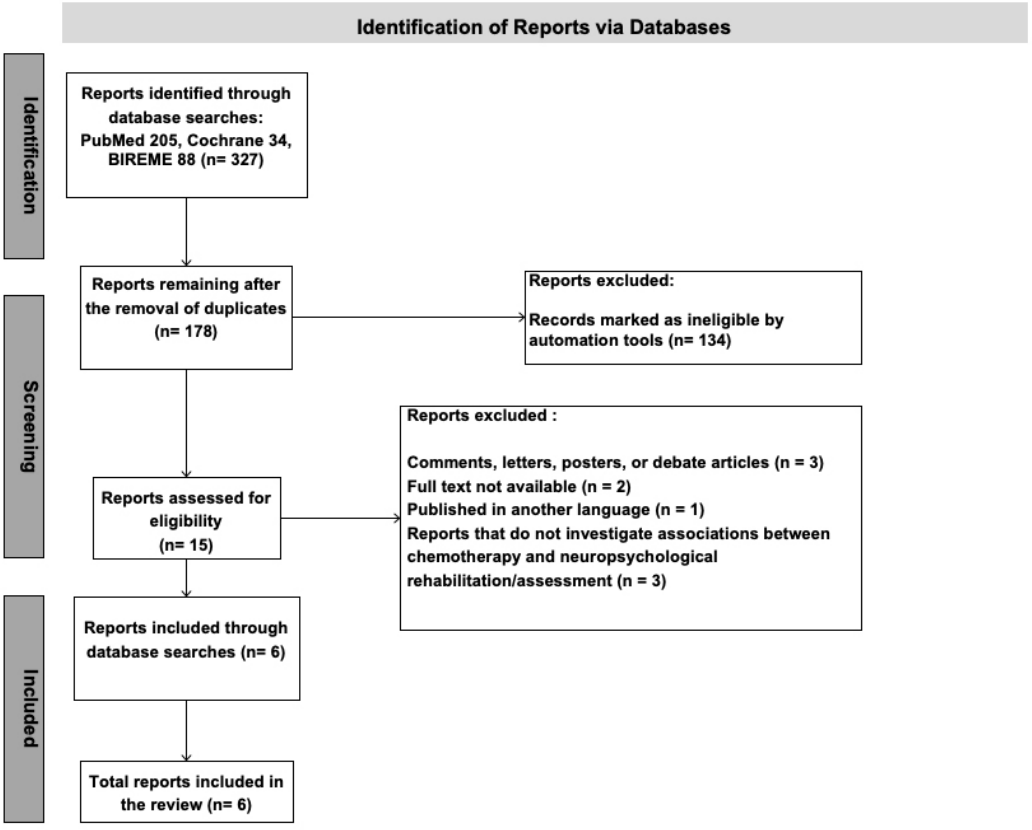

Figure 1. PRISMA diagram showing selection of articles

Quality Assessment

According to RoB2, studies were evaluated for bias in randomization, intervention deviations, missing data, outcome measurement, and selective reporting. Three studies presented biases across multiple domains, while two studies had high biases, affecting reliability (see Figure 2).

Characterization of Patients

The studies primarily included middle-aged women (approximate mean age of 51.5 years), with half having higher education, however, the studies presented the participants' ages and education inconsistently, with some reporting the mean age, others the median, or having the variables sorted categorically. Ethnic data were reported in one study, where 70.5% identified as white. Breast cancer was the most prevalent cancer type (2/6 studies focused solely on it). All studies included participants who had completed cancer treatment at least two months prior, with most undergoing multimodal treatment (e.g., surgery, immunotherapy, radiotherapy, or hormone therapy, see Table 2).

Assessment Instruments

Of the selected studies, 83.3% (5/6) used objective cognitive assessments, however, these instruments ranged from neuropsychological tests to computerized tools (Bray et al., 2017; Dos Santos et al., 2020; Mihuta et al., 2018; Poppelreuter et al., 2009; Vardy et al., 2023). All studies assessed working memory and information-processing speed. Other functions assessed that were not present in all studies included language, visual and verbal learning, attention, verbal memory, and executive function. The Functional Assessment of Cancer Therapy Cognitive Function version 3 (FACT-COG V3) was the most common self-report instrument, used in 83.3% (5/6) of studies (Bray et al., 2017; Dos Santos et al., 2020; Mihuta et al., 2018; Myers et al., 2020; Vardy et al., 2023), to assess cognitive complaints linked to cancer and treatment. Anxiety, depression, and quality of life were also assessed using diverse instruments (see Table 3).

Cancer Treatments

All participants underwent chemotherapy, as required for inclusion. In five studies, patients had completed their treatment, while three participants included were still undergoing hormone therapy. Surgery was noted in three studies, radiotherapy in all, and hormone therapy in five. Only two studies specified chemotherapy drugs (e.g., anthracyclines, platinum compounds, CMF-based regimens, Taxanes).

Rehabilitation Intervention

Five out of six studies used computerized rehabilitation programs. Protocols ranged from 4 to 9 weekly sessions, lasting 40 minutes to 2 hours. Four studies implemented face-to-face rehabilitation guided by a professional, with one adapting to virtual formats due to COVID-19. Programs typically included cognitive training, psychoeducation, and daily life skill training (see Table 3). For the studies that implemented these activities, it is important to note that cognitive training focused on exercises that were adapted or individualized to improve skills such as processing speed, attention, and memory. In these training sessions, participants engaged in computerized or in-person tasks, practiced daily life activities, planned and participated in activities, and recalled complex verbal information (Bray et al., 2017; Dos Santos et al., 2020; Mihuta et al., 2018; Myers et al., 2020; Poppelreuter et al., 2009; Vardy et al., 2023).

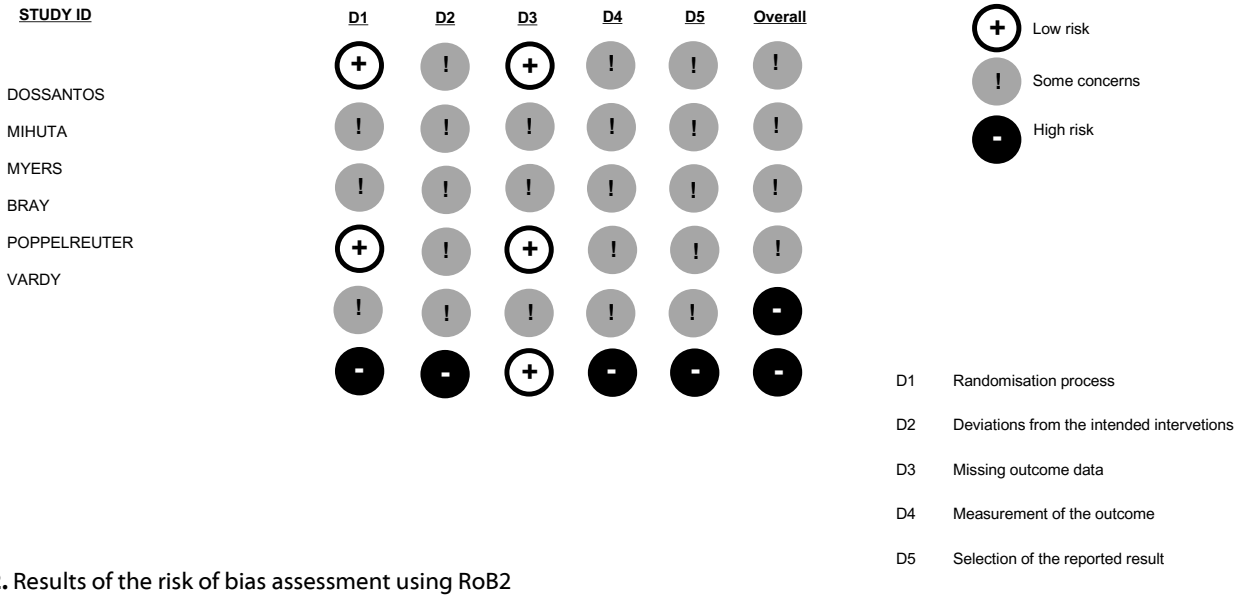

Figure 2. Results of the risk of bias assessment using RoB2

Table 2. General descriptions of studies included in this review.

Authors and Year	Country and Journal	Participants Groups				Type	Other treatments	Chemotherapy	Design	Objetive
		Experimental 1	Experimental 2	Control 1	Control 2					
Bray et al., (2017)	J of Clin Onc (Australia)	N: 121 (96% W) A:52 (#)	-	N: 121 (94% W) A: 54 (#)		89% breast cancer 5% colorectal cancer	67,8% Radiotherapy 70.8% Hormone T. 22.3% Immune T.	CC: 27 months (#)	Randomized controlled trial	Evaluate a cognitive rehabilitation program (Insight) and compare it with standard care.
Dos Santos et al., (2020)	Cancer (France)	N: 55 (96.4% W) A:51.7 (#)	-	N: 56 (94.6% W) A: 50.9 (#)	N: 56 (96.4% W) A: 50.7 (#)	84% breast cancer	91% Surgery 79% Radiotherapy 70% Hormone T.	CC: 10,6 months (#) Type: Sequencial	3-arm randomized trial with two active control arms	Evaluate the impact of computer-assisted CR on subjective and objective cognition, QOL, anxiety, and depression.
Mihuta et al., (2018)	Eur. J. Cancer Care (Australia)	N:12 (100.0% W) A: 45.4 (±10.3)	-	N: 16 (75.0% W) 47.6 (±10.0)	N: 15 (73.3% W) 45.9 (±7.4)	50% breast cancer 16,7% Lymphoma 8.3% Bowel 8.3% Endometrial 8.3% PMP appendix 8.3% SCC vulva	83,3% Surgery 58.3% Radiotherapy	CC: 52.3 months (±46.8)	Randomized controlled trial	Evaluate the efficacy of a web-based cognitive rehabilitation intervention in survivors of adult-onset cancer and a sample of non-cancer community dwelling adults.
Myers et al., (2020)	Arch. Phys. Med. Rehabil (EUA).	N: 26 (100.0% W) A:56.9(±11.5)	-	N: 26 (100.0% W) A:54.3(±10.1)	-	100% breast cancer	64,4% Radiotherapy 62,3% Endocrine T. 100% Surgery	CC: 404 days (±335)	Prospective, nonblinded, wait-list controlled pilot study	Quantify the effect of a psychoeducation-based cognitive rehabilitation intervention on breast cancer survivors' self-report of cognitive function.

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Authors and Year	Country and Journal	Participants Groups				Type	Other treatments	Chemotherapy	Design	Objetive
		Experimental 1	Experimental 2	Control 1	Control 2					
Poppelreuter, Weis, & Bartsch (2009)	J. Psychosoc. Oncol. (Germany)	N: 33 (100.0% W) A: 49.19 (±7.71)	-	N: 32 (100.0% W) A: 49.19 (±7.71)	N: 25(100.0% W) A: 49.19 (±7.71)	100% breast cancer	89.6% Radiotherapy 70.8% Antihormonal T.	CC: 2.06 months (±2.78) Drug - anthracyclines (docetaxel or paclitaxel)	Two-arm randomized controlled study	Examine the need for cognitive training and the differentiated evaluation of the effectiveness of two specific forms of training.
Vardy et al. (2023)	J. of Cancer Survivorship (Australia)	N: 24 (100% W) A: 52.2 (±6.1)	N: 21 (95.2 W) A: 56.7 (±8.6)	N: 20 (100% W) A: 54.8 (11.5)	-	92.31% breast cancer 6.15% colorectal cancer 1.54% cancer gyneacological	70.77% Radiotherapy 72.31% Hormone T.	CC: 20,7 months (#)	Randomized controlled trial	Evaluate two cognitive rehabilitation programs used in non-cancer populations against standard-of-care control in solid tumor survivors self-reporting cognitive impairment after chemotherapy.

Abreviations: E: Experimental Group; CG: Control Group; A: Age; W: Women; # - standard deviation was not informed; CC: chemotherapy conclusion, the median time from chemotherapy completion.

Table 3. Description of the evaluation process, intervention and findings of the studies included in the review

Authors and year	Neuropsychological instruments	Self-Reporting instruments	Moments of the assessment	Experimental Group intervention	Control Group Intervention	Duration	Primary outcomes	Secondary Outcomes
Bray et al., (2017)	Cogstate.	Functional Assessment of Cancer Therapy Cognitive Function version 3 (FACT-Cog) #; Two-item European Organization for Research and Treatment of Cancer (QLQ-C30); Cognitive Functioning scale 12-item General Health Questionnaire; QOL (FACT-General); FACT-Fatigue subscale; 14-item Perceived Stress Scale.	T1: baseline; T2: after the 15-week intervention; T3: 6 months later.	Web-Based Cognitive Rehabilitation Program – using the Insight from Posit. It is a computerized neurocognitive learning program that is based on the neuroplasticity model. It uses adaptive exercises targeting processing systems aimed at improving cognition through the speed and accuracy of an information processing Science program.	Standard care.	4 sessions of 40 minutes/ week for 15 weeks, totaling 40 hours	There were statistically significant differences across all FACT-COG subscales in the intervention group compared to the control group, which assessed PCI, PCA, and QOL; Less perceived cognitive impairment in the intervention group at T2; Perceived cognitive abilities were significantly better in the intervention group; Differences remained at T3.	There were no major differences in objective neuropsychological test results between the groups; There were lower levels of anxiety/ depression in the intervention group at T2, with no significant difference at T3; Lower levels of fatigue in the intervention group at T2, with no significant difference at T3; No difference in global QOL between the groups at T2, but the intervention group had better global QOL at T3; Benefits in perceived stress in the intervention group at T2 and T3.

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Authors and year	Neuropsychological instruments	Self-Reporting instruments	Moments of the assessment	Experimental Group intervention	Control Group Intervention	Duration	Primary outcomes	Secondary Outcomes
Dos Santos et al., (2020)	Grober and Buschke D2 test; Verbal fluency test; Trail Making Test; Wechsler Adult Intelligence Scale IV (WAIS IV).	Functional Assessment of Cancer Therapy–Cognitive Function; Functional Assessment of Cancer Therapy General (FACT-G) #; Functional Assessment of Cancer Therapy-Anemia (FACT-An); The Spielberger State-Trait Anxiety Inventory; The Center for Epidemiologic Studies Depression Scale.	T0: baseline (all instruments); T1: completed 1 month of intervention (Only subjective cognitive assessment); T2: completed 2 month of intervention (Only subjective cognitive assessment); T3: at the end of the program 3 months later (all instruments);	Computer-assisted cognitive rehabilitation with a neuropsychologist – using the RehaCom software. It is a modular interactive program designed to train cognitive abilities.	CG 2: home cognitive self-exercises CG 3: phone follow-up	E: 9 sessions (45-60 minutes) over 3 months; CG 2: 9 sessions 30-60 minutes per week; CG 3: Called 9 times over 3 months	Despite the improvement identified in all subscales of the FACT-Cog, which assesses perceived cognitive impairment (PCI), perceived cognitive abilities (PCA) and their impact on QOL, no statistically significant differences were found between the groups. However, the mean difference in PCI scores between T0 and T3 was statistically significant in the experimental group compared to the two control groups.	A statistically significant improvement in working memory was found in the experimental group; No significant difference was demonstrated for the other domains of objective cognition; Depression scores improved significantly in the experimental group.
Mihuta et al., (2018)	WebNeuro online cognitive test battery.	Functional Assessment of Cancer Therapy—Cognitive Function (FACT-Cog) #; Brief Assessment of Prospective Memory (BAPM) #; European Organization for Research and Treatment of Cancer—Quality of Life Questionnaire (EORTC QLQ-C30) #; Brief Illness Perception Questionnaire (BIPQ); Kessler Psychological Distress Scale (K10).	T1: baseline; T2: post-intervention or 4 weeks after the baseline assessment for the waitlist group; T3: 3-month follow-up.	The eReCog (Online Responding to Cognitive Concern) is an online cognitive rehabilitation program based on CBT principles that offer adult cancer survivors psychoeducation on cognitive dysfunction associated with cancer treatment, skills training for memory and attention, relaxation training, tips for improving sleep hygiene, and weekly homework tasks.	CG 1: Same intervention as the experimental group CG 2: wait-list	4 weekly sessions lasting about 2 hr each	The cancer group showed a trend towards reporting reduced prospective memory (PM) failures at both T2, and T3, the noncancer treatment group reported reduced PM failures at T2 only, no changes were reported by the CG2. Despite not reaching statistical significance, the cancer group showed a significant improvement in perceived cognitive impairment (PCI) from T1 to T2.	Attention showed a significant interaction whereby the cancer group and the non-cancer waitlist group improved over time but the non-cancer treatment group declined. The cancer group reported a significantly higher perception of threat associated with illness than both the non-cancer treatment group and the waitlist group.

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Authors and year	Neuropsychological instruments	Self-Reporting instruments	Moments of the assessment	Experimental Group intervention	Control Group Intervention	Duration	Primary outcomes	Secondary Outcomes
Myers et al., (2020)	No objective measurement instruments were used.	The Functional Assessment of Cancer Therapy-Cognition (FACTCog) #; Patient-Reported Outcomes Measurement Information System (PROMIS); PROMIS Applied Cognition General Concerns (PROMIS-29); UCLA Loneliness Scale.	T1: Baseline; immediately after week 6 of Haze; T2: 1 month; T3: 6 months; T4: 12 months later. Data were collected from wait-list controls at baseline, T1, and T2.	Haze intervention – Psychoeducation Based Cognitive Rehabilitation Intervention. Components: Intervention presentation, class exercises, discussion, and homework exercises.	Wait-list	6 weekly sessions lasting 2.5-hour each class	The intervention group participants demonstrated more improvement than controls between baseline and T1 for perceived cognitive abilities (PCA) and quality of life (QOL); The intervention group also demonstrated more improvement for perceived cognitive impairments (PCI) and QOL between baseline and T2.	Improvement in the score of cognitive functions evaluated by the PROMIS instrument and in the loneliness scores. Loneliness severity was strongly associated with reports of worse perceived cognitive function (PCF) for both the intervention and wait-list control participants.
Poppelreuter, Weis, & Bartsch (2009)	Computerized Test Battery for Attentional Performance (TAP) #; Rivermead Behavioral Memory Test (RBMT) #; Wechsler Memory Scale-R (WMS-R) #; Learning and Memory-Test (LGT) #.	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) #; Multidimensional Fatigue Inventory (MFI); Hospital Anxiety and Depression Scale (HADS); Questionnaire of Self-Perceived Deficits in Attention (FEDA).	T1: Baseline; T2: At the end of rehabilitation; T3: 6 months later.	Group 1 - Neuropsychological Training Group (NPT) is a functional cognitive training skills to the demands of everyday life as realistically as possible. Group 2 - computer-based training (PC) software that uses several tasks addressing specific dimensions of attention and memory according to the parameters of the neuropsychological test battery used in the study.	CG 2: standard rehabilitation program	All groups: part in 4 sessions lasting 1-hour	No specific intervention effects improvement was found. The control group (without specific training) improved in the same manner as both training groups. There was a significant improvement in performance in most of the neuropsychological parameters during the rehabilitation program in all three study groups. It was observed that 47.1% of the patients presented signs of possible cognitive deficits and the need for training.	A strong general trend towards improvement in neuropsychological test scores was observed, but our data also reveal a subgroup of patients showing clinically relevant cognitive deficits about a year after chemotherapy.

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Authors and year	Neuropsychological instruments	Self-Reporting instruments	Moments of the assessment	Experimental Group intervention	Control Group Intervention	Duration	Primary outcomes	Secondary Outcomes
Vardy et al., (2023)	Wide Range Achievement Test (WRAT) 3 Reading test; Controlled Oral Word Association Test (COWAT); Trail Making Test Part B; Wisconsin Card Sorting Test (WCST) (32 item); Stroop Colour and Word; Speed of information processing: Symbol Digit Modalities Test (SDMT); Trail Making Test Part A; Wechsler Memory Scale (WMS) III Digit Span; Wechsler Adult Intelligence Scale (WAIS) III Letter-Number Sequencing; WMS-III Spatial Span; Hopkins Verbal Learning Test-Revised (HVLT-R); Brief Visuospatial Memory Test-Revised (BVMT-R); Grooved pegboard.	Functional Assessment of Cancer Therapy Cognitive Function version 3 (FACT-COG) questionnaire; Hospital Anxiety Depression Scale (HADS); FACT-General (G); FACT-Fatigue (F) subscale; Active Australia Exercise Questionnaire.	T1: Initial assessment after the 6-week intervention. T2: 6 months T3: 12 months	Group 1 - Attention Process Training (APT) group: a structured neurocognitive learning program that used repetitive computerized exercises designed to practice attention tasks. Group 2 - Compensatory Strategies Training (CST) group: structured sessions focused on compensatory strategies, education and feedback, as well as stress management and psychosocial support.	Standard care.	2h weekly small group session for 6 weeks	No significant differences were found between the intervention groups and the control group for cognitive symptoms, using ANCOVA models adjusted for baseline scores.	There was improvement in cognitive symptoms and neuropsychological test scores over time in all groups, with a non-significant trend towards a greater reduction in the proportion of participants with impairment in the intervention groups post-treatment.

Abreviations and simbols: #: primary instrument defined by the study;

Regarding psychoeducation, it was commonly integrated with behavioral practices and intervention processes, focusing on cognitive dysfunctions resulting from cancer treatment, their implications, and potential coping strategies (Mihuta et al., 2018; Myers et al., 2020; Vardy et al., 2023).

Daily life skill training involved interventions that utilized relaxation techniques and goal-setting strategies (Mihuta et al., 2018; Vardy et al., 2023) along with sleep hygiene tips (Mihuta et al., 2018), stress management (Vardy et al., 2023), and teaching compensatory strategies (Dos Santos et al., 2020; Poppelreuter et al., 2009; Vardy et al., 2023) aimed at improving performance in daily activities. Some protocols also included homework assignments (Mihuta et al., 2018; Myers et al., 2020; Vardy et al., 2023) and psychosocial support (Vardy et al., 2023) as part of the rehabilitation intervention process.

Outcomes of Intervention Programs

Among the studies, five (83.3%) reported favorable intervention outcomes, though only three (50%) demonstrated statistically significant improvements. The FACT-Cog V3 self-report scale showed significant reductions in perceived cognitive impacts, increased perceived cognitive abilities, and quality-of-life enhancements in four studies. One study identified improvements in prospective memory in the intervention group using the Brief Assessment of Prospective Memory (BAMP) tool. Only two studies showed significant improvements in objective cognitive measures. Mihuta et al. (2018) reported working memory gains in the experimental group, measured with WAIS IV. Dos Santos et al. (2020) found improved attention scores assessed with WebNeuro. Of these studies, 5 (83.3%) indicated that cognitive interventions not only promoted significant improvements in perceived cognitive functions but also contributed to the reduction of emotional symptoms such as anxiety, depression, and fatigue. The approaches varied, including computer-assisted cognitive rehabilitation programs, neuropsychological training, psychoeducation, and techniques that incorporated relaxation and goal setting.

DISCUSSION

Cancer treatments are widely recognized for their potential to enhance recovery and increase survival rates; however, the employment of these methods has been associated with adverse effects that can diminish patients' quality of life (Oliveira et al., 2023; Shaw et al., 2021; Syarif et al., 2021; Yang & Von Ah, 2024). Concerns regarding the side effects of chemotherapy emerged circa 1970, but in recent years, the number of studies has increased substantially (Skurlova et al., 2024; Untura & Rezende, 2012).

Cognitive alterations caused by chemotherapy prevail as a critical area of investigation since the relationship between the effects of chemotherapy and its mechanisms of action on cognition is still not completely clear. Cognitive impairment directly affects patients' lives, resulting in reduced quality of life (Skurlova et al., 2024; Untura & Rezende, 2012), impacting individuals' ability to independently perform daily activities, maintain social relationships, and even compromising job performance (Skurlova et al., 2024; Untura & Rezende, 2012).

Based on these findings, we identified a broad spectrum of cognitive function assessment protocols and cognitive or neuropsychological rehabilitation programs. Limited similarity was observed among the instruments used to measure cognitive impairment post-chemotherapy, with working memory and processing speed being the only cognitive functions consistently assessed across these protocols. Regarding the intervention process, we observed that a wide range of programs were under investigation.

All patients in the studies were undergoing adjuvant treatment in addition to chemotherapy, and there were no studies that examined chemotherapy as an exclusive treatment, which may impede the identification of the precise cause of cognitive impairment. Furthermore, as is well established in the scientific literature, depression and anxiety may be associated with cognitive changes (Culpepper et al., 2017; Perini et al., 2019). Thus, it is necessary to consider that the entire process of diagnosis, treatment, and experience of a disease such as cancer can be stressful and facilitate the development of these symptoms.

The included studies highlighted the presence of symptoms of depression and/or anxiety, in addition to their impacts on patients' quality of life, which may support the hypothesis that the onset of cognitive impairment is also related to these conditions. These findings reinforce the hypothesis that these symptoms strongly influence self-report scales of perceived cognitive impairments, and consequently, favorable results for neuropsychological intervention programs.

Bray et al. (2017), Mihuta et al. (2018), and Vardy et al. (2023) studies show improvements in cognitive functions correlated with a decrease in levels of anxiety and depression, as well as an enhancement in the participants' quality of life. These results suggest that the interventions not only improved cognitive well-being but also had a positive impact on the emotional aspect of life. In Bray et al. (2017), the FACT-Cog V3 scale was used to assess participants' perceptions of their cognitive impairment before and after the intervention. This assessment revealed significant reductions in perceived cognitive impacts, reflecting a sense of greater cognitive ability and control over daily activities, which in turn helped alleviate the participants' emotional burden. Such findings suggest that cognitive interventions, by improving cognitive function, can have a positive impact on emotional well-being.

Understanding emotional functioning is considered one of the central elements in rehabilitation, significantly influencing the quality of patient care (Wilson, 2008). In this regard, interventions derived from Cognitive Behavioral Therapy (CBT) have been identified as effective alternatives, used not only to

stimulate the development of coping strategies and management of cognitive deficits in patients (Mateer et al., 2006; Yang & Von Ah, 2024), but also for the treatment of anxiety and depression (Mateer et al., 2006). Moreover, the strategies of this approach, when adapted, are also capable of promoting improvements in psychological functioning and self-monitoring skills in these patients (Lopes et al., 2023).

The study by Cicerone et al. (2008) examined the effectiveness of two neuropsychological rehabilitation programs, one focused on a holistic approach and the other on a standard, multidisciplinary treatment, in patients with Traumatic Brain Injury (TBI). The holistic rehabilitation group integrated strategies for cognitive deficits, emotional difficulties, interpersonal behaviors, and functional skills, with an emphasis on metacognition (self-monitoring and self-regulation) and emotional regulation. The results showed that, although both groups reported improvements in cognitive factors, participants who underwent a holistic and comprehensive approach demonstrated better management of their cognitive and emotional symptoms, as well as higher levels of perceived self-efficacy.

Interventions showed improvements in cognitive symptoms compared to standard care procedures. Regarding performance, attention (Mihuta et al., 2018) and working memory (Dos Santos et al., 2020) stand out as areas of significant improvement, leading to a reduction in cognitive impairment symptoms in patients. Furthermore, some self-report measures indicate a reduction in psychological symptoms such as depression and anxiety (Dos Santos et al., 2020). These results suggest that the programs had a positive impact on cognitive and psychological functioning; however, despite the improvement in stress symptoms and quality of life of these patients, the extent to which these results can be generalized to their daily lives remains uncertain (Bray et al., 2017).

The reduction in cognitive, anxiety, and depression symptoms evidenced by self-report assessments may be attributed to a supportive environment where these feelings are validated and accepted, presenting itself as a strong hypothesis to mitigate psychological alterations in interventions. Another noteworthy point is the improvement in loneliness scores (Myers et al., 2020).

The studies reviewed exhibited considerable diversity in the selection of assessment instruments, with no single tool repeated across studies, thereby complicating direct comparisons. Dos Santos et al. (2020) identified a statistically significant improvement in working memory between the pre- and post-intervention phases; however, other studies noted only subtle changes without statistical significance between groups. This highlights a discrepancy, as statistically significant findings were often reported in self-report measures (4 out of 6 cases).

This inconsistency warrants careful examination, as the absence of significant cognitive assessment results does not necessarily imply that the impacts perceived by patients are trivial. Other factors, such as the treatment experience and its effect on quality of life, may amplify the perception of cognitive deficits (Culpepper et al., 2017; O'Farrell et al., 2017; Perini et al., 2019). This issue underscores a potential limitation in this research area, particularly regarding the lack of baseline cognitive function data (i.e., cognitive assessments conducted before chemotherapy or adjuvant therapies). Future studies should prioritize selecting instruments with greater sensitivity to detect subtle changes across the pre-treatment, post-treatment, and rehabilitation phases.

CONCLUSION

This study reviews existing literature on patients who developed cognitive deficits following chemotherapy and subsequently participated in cognitive or neuropsychological rehabilitation. Our findings reveal that, despite the variety of neuropsychological rehabilitation protocols employed in clinical settings, there is: a) a lack of consistency in standardizing research protocols before and after interventions; b) inconsistency in the measures and assessment tools used; and c) limited significant effects of rehabilitation programs relative to subjective measures.

Given the impact of chemotherapy-related cognitive impairment on patients' quality of life, more research is essential to clarify the relationship between chemotherapy and cognitive decline, as current findings remain inconclusive. Developing structured cognitive and neuropsychological rehabilitation programs is crucial to support patients in managing these challenges.

This study also highlights the diversity of rehabilitation programs and assessment protocols, which complicates cross-study comparisons. Further research should focus on rigorously evaluating existing interventions and developing a standardized evaluation protocol that would facilitate comparative analysis across diverse clinical contexts

Limitations

Although this review followed PRISMA criteria, the findings may not fully reflect the clinical reality for chemotherapy patients undergoing rehabilitation. The limited number of articles available highlights a scarcity of studies on this subject. This research aimed to investigate a broad population of cancer patients to ensure generalization; however, most studies focused predominantly on women with breast cancer. Additionally, the wide variability in protocols and highly specific subject groups complicates efforts to identify a standard intervention protocol.

Implications for Rehabilitation

This study identified work on cognitive rehabilitation protocols for patients with chemotherapy-induced cognitive deficits. However, the lack of a standardized rehabilitation program with consistently effective outcomes underscores the variety of protocols in the literature, which often yield

inconclusive results after intervention. Consequently, research is urgently needed to focus on standardized rehabilitation programs, allowing assessment of their effectiveness across diverse settings and patient groups affected by various cancer types and treatments. To improve the reliability of intervention outcomes, it is also recommended to assess patients' cognitive functions before beginning chemotherapy. This would provide a comprehensive baseline for understanding cognitive profiles and enable more precise detection of post-treatment and post-intervention changes

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