Original Article

Meta-analysis of neurocognitive rehabilitation for cognitive dysfunction among pediatric cancer survivors

ABSTRACT

Cancer and its treatment significantly affect the cognitive functioning of pediatric cancer survivors. This meta-analysis aimed to examine the effects of neurocognitive rehabilitation interventions on the cognitive functioning and intellectual performance of pediatric cancer survivors. Four databases were searched until December 15, 2021. RevMan 5.4 was used to analyze the effects of neurocognitive rehabilitation interventions on the cognitive functioning of pediatric cancer survivors. Ten eligible randomized controlled trials were initially identified, and nine of these were included in the meta-analysis. For the working memory outcome, the pooled effect results favored study interventions and had statistical significance at postintervention assessment ($Z = 2.24$, $P = 0.03$). For the attention outcome, there were significant statistical differences at postintervention and 3/6-month follow-up assessment ($Z = 2.72$, $P = 0.007$ and $Z = 10.45$, $P < 0.001$, respectively). For the executive functioning outcome, there were significant statistical differences at postintervention and 3/6-month follow-up assessment ($Z = 2.90$, $P = 0.004$ and $Z = 14.75$, $P < 0.001$, respectively). For the academic/intellectual performance secondary outcome, the pooled overall effects of study interventions on the academic/intellectual outcome were positive at postintervention and follow-up assessment (Ps < 0.001). No studies reported any adverse events related to neurocognitive and educational interventions. This meta-analysis found that neurocognitive rehabilitation interventions improve the working memory, attention, and executive functioning of pediatric cancer survivors at postintervention and short-term follow-up. Neurocognitive rehabilitation also has positive effects on the academic/intellectual performance of this study population during a vulnerable period in their development.

KEY WORDS: Cognitive functioning, meta-analysis, neurocognitive rehabilitation, pediatric cancer survivors

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INTRODUCTION

More than 400,000 children worldwide are diagnosed with cancer annually, and a child is diagnosed with cancer every 3 min.[1] In high-income countries, such as the United States, the estimated 5-year net survival rate for pediatric cancers is 79.85%, and the global 5-year survival rate is 56%.[1] Among all types of pediatric cancer, the two most common forms are brain tumors and acute lymphoblastic leukemia (ALL).[2] With an increased number of pediatric cancer survivors, two-thirds of this cancer survivor population report at least one cancer-related sequela, such as cognitive dysfunction,[3-5] which can adversely affect their health and academic development/growth.[3,6]

Previous research has estimated that one-third of pediatric cancer survivors report cognitive dysfunction.[7] Among pediatric brain tumor survivors, the prevalence of cognitive dysfunction is as high as 50%–80%.[8] Cognitive dysfunction includes various aspects of impairment in working memory, attention, executive functioning, and information processing speed, all of which have negative effects on the learning abilities, academic achievement, and long-term development of pediatric cancer survivors, including their educational and employment attainment.[2,8,9] Neurocognitive rehabilitation interventions effectively diminish cognitive dysfunction among pediatric cancer survivors.[2,10-13] These intervention programs utilize cognitive and/or behavioral skills acquisition approaches demonstrated to improve the cognitive functioning and academic achievement of pediatric cancer survivors.[2]

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One meta-analysis compared the academic/intellectual outcomes of pediatric cancer survivors with ALL to those of controls without a history of cancer.[14] In terms of study subjects, this meta-analysis only included pediatric cancer survivors with ALL. In terms of study types, it only included observational studies and failed to include any intervention study.[14] Krull *et al.*[2] provided a comprehensive review of all aspects of cognitive dysfunction, including the prevalence and pattern, associated factors, neurochemical biomarkers of cognitive deficits, cognitive outcome assessment, and possible interventions, to facilitate rehabilitation for long-term pediatric cancer survivors, including survivors of the two most common cancer types, namely brain tumor and ALL. However, this review did not quantify the effects of neurocognitive rehabilitation programs on the cognitive and academic outcomes of pediatric cancer survivors.

Therefore, this current meta-analysis aimed to examine the effects of neurocognitive rehabilitation interventions on the cognitive functions of pediatric cancer survivors and whether cognitive remediation interventions improve the academic/intellectual performance of this study population.

SUBJECTS AND METHODS

Search strategy and data resources

This meta-analysis involved a literature search in four electronic databases—PubMed, EMBASE, Scopus, and PsychINFO—until December 15, 2021. The search terms used a combination of keywords and medical subject headings. The search strategies are listed in Appendix 1.

Eligibility criteria

Studies involving pediatric patients and/or survivors with brain tumors or ALL were included in this meta-analysis, as these are the most common types of childhood cancer. In line with the conventional age-related definition, pediatric cancer survivors were defined as children ages <18 years. The examined interventions included all neurocognitive rehabilitation programs, such as neurocognitive and psychoeducational interventions. The controls included standard/usual care, waitlist controls, and other supportive care interventions. The primary outcomes included cognitive outcome measures, and the secondary outcomes included academic/intellectual outcomes and any adverse effects directly related to interventions. In terms of study types, only randomized controlled trials (RCTs) were included.

Data extraction

Two of the authors (X.W. and F.H.) independently conducted data extraction for each RCT. Both authors mainly extracted the characteristics, including key information about the study population, interventions, outcome measures, and the results of primary and secondary outcome measures at postintervention and follow-up assessments. If there was any disagreement involving data extraction, the final author of this manuscript (A.S.K.C.) was always involved in the discussion to achieve agreement.

Risk of bias assessment

The study used the Cochrane Risk of Bias Assessment tool[15] for the methodological quality assessment. The steps in the assessment were similar to those in the data extraction process. Two authors (L.Y. and H.H.) conducted the risk of bias assessment for each included RCT independently, and any disagreements were discussed with the third author (Y.L.) to reach a consensus.

Data synthesis and analysis

The Cochrane Collaboration's Review Manager (RevMan 5.4) was used for quantitative data synthesis and estimating the pooled effects of study interventions.[15] If data for standard deviations were missing, they were calculated using standard errors or other related information, such as 95% confidence intervals (95% CIs), using the RevMan Calculator.[16] The heterogeneity of the included trials was calculated with χ^2 test and I^2 statistics. $P < 0.1$ (χ^2) and $I^2 > 50\%$ are indicators of statistical heterogeneity.[17] If an obvious indication of heterogeneity occurred, the estimations of the intervention effect size were made using the random-effects model; otherwise, the estimation of the intervention effect size was made using the fixed-effects model. The pooled effects of study interventions were assessed using $P < 0.05$, indicating statistical significance.

RESULTS

The methodology of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 was followed.[18] Figure 1 presents the full study selection procedure. In total, 10 of 125 extracted studies were initially selected for the meta-analysis. However, 1 of these 10 studies was a pilot RCT without sufficient information for pooling study outcomes;[19] so, only nine RCTs were included in this meta-analysis.[10-12,20-25]

Characteristics of included studies

Table 1 presents the characteristics of nine RCTs included in the meta-analysis. Data were organized under the headings of author and year, study participants, study interventions, outcome measures, and major findings. The number of study participants varied from 20 to 161. The age ranges of pediatric cancer survivors were mainly from 6 to 18 years. Of the nine RCTs, six adopted cognitive training interventions, whereas the remaining three used the following types of intervention: cognitive rehabilitation, neurofeedback, and education. The key cognitive outcome domains included working memory, attention, and executive functioning. Academic/intellectual performance was mainly measured by the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV; Table 1).

Quality of study methods

Figure 2a presents a summary of the risk of bias assessment,

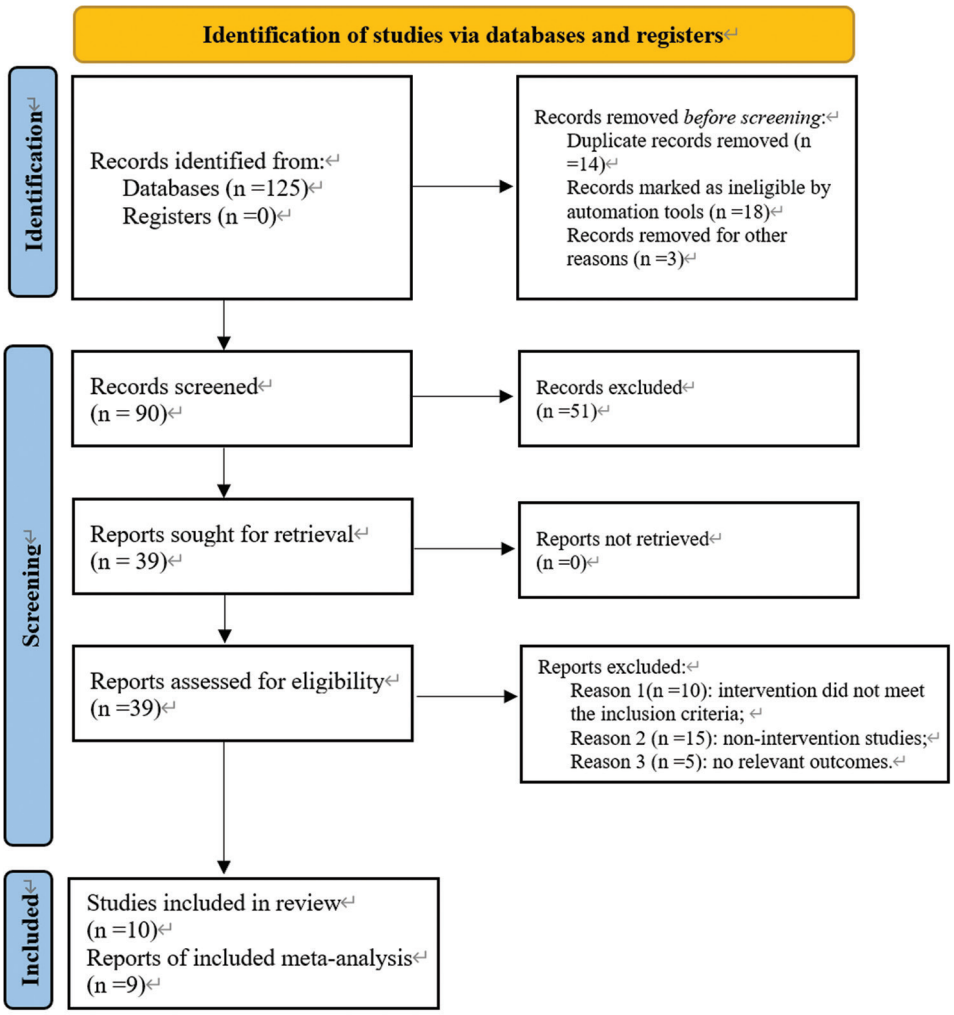

Figure 1: PRISMA 2020 flow diagram of the study selection

and Figure 2b presents the bias assessment risk of each RCT. Overall, all nine included RCTs had a low risk of bias. Only in the domain of blinding study subjects or research personnel did these studies have a high risk of bias. Of the nine included trials, only one used a strategy to blind the study subjects and/or research personnel by providing two versions of the intervention program, which varied from the levels of the intervention dose.[10]

Effects of study interventions on primary outcomes

In terms of primary outcomes, all included trials reported improvements in cognitive outcomes, including working memory, attention, and executive functioning. In Figure 3a to c, comparisons of the working memory outcome reported that the pooled effects were in favor of study interventions; however, there was only statistical significance at postintervention assessment ($Z = 2.24$, $P = 0.03$; Figure 3a). The changes in scores for working memory and follow-up assessment of working memory at 3/6-month follow-up had no statistical significance ($Z = 1.70$, $P = 0.09$ and $Z = 1.45$, $P = 0.15$, respectively, Figure 3b and c). In terms of the attention outcome, there were significant statistical differences at postintervention and 3/6-month follow-up assessment [Figure 4a and b]. Six trials assessed the effects of neurocognitive interventions on pediatric cancer survivors' attention at postintervention; the reported standard mean difference (SMD) was 0.81 (95% CI, 0.23–1.40; $Z = 2.72$, $P = 0.007$; Figure 4a). Three trials reported attention outcomes at follow-up; the reported weighted mean difference (WMD) for the attention outcome was 1.38 (95% CI, 1.12–1.64) at 3/6-month follow-up [Figure 4b]. In terms of executive functioning outcomes, six trials assessed the effects of neurocognitive interventions on pediatric cancer survivors' executive functioning at postintervention, with an SMD of 1.06 (95% CI, 0.34–1.77; $Z = 2.90$, $P = 0.004$; Figure 5a), and three trials assessed executive functioning outcomes at follow-up, with a WMD of 1.76 (95% CI, 1.53–2.00) at 3/6-month follow-up [Figure 5b].

Effects of study interventions on secondary outcomes

In terms of secondary outcomes, all included trials reported improvements in academic/intellectual performance at

Table 1: Characteristics of the included nine RCTs

Author (year)	Study participants	Study interventions	Outcome measures	Major findings
Benzing *et al*. (2020)	69 pediatric cancer survivors ages 7-16 years old	8-week working memory training and exergaming interventions, each training course including three 45-min training sessions per week	Executive functions; intelligence, planning, memory, attention, processing speed, and motor abilities	Subjects in the intervention group had a linear improvement in visual working memory compared to the control group
Bulter *et al*. (2008)	161 childhood cancer survivors ages 6-17 years	Cognitive remediation program: a total of up to 20 two-hour weekly sessions over 4-5 months, including hierarchically graded massed practice, strategy acquisition, and cognitive behavioral interventions	A battery of academic achievement/neurocognitive tests: brief focused attention; working memory; memory recall; learning/learning strategies	Subjects in the intervention group had potentially beneficial treatment for childhood cancer survivors, who accepted intervention with improved attention and statistically significant increases in academic achievement
Conklin *et al*. (2015)	68 survivors of childhood ALL or brain tumor ages between 8 and 16 years	Computerized cognitive training: a total of 25 homely training sessions, one session per week, phone-based coaching	WISC-IV integrated spatial span, digit span, and letter-number sequencing for attention and processing speed; BRIEF for working memory; and CPRS-3 for executive function	Subjects in the intervention group reported greater improvement than controls on measures of working memory with ES of 0.84, attention with ES of 0.65, and processing speed with ES of 0.61 and showed greater reductions in reported executive dysfunction
Conklin *et al*. (2017)	68 survivors of childhood ALL or brain tumor ages between 8 and 16 years	Computerized cognitive training: a total of 25 homely training sessions, one session per week, phone-based coaching	WISC-IV integrated spatial span, digit span, and letter-number sequencing for attention and processing speed; BRIEF for working memory; and CPRS-3 for executive function	Subjects in the intervention group with cognitive benefits were maintained 6 months after the intervention, working memory and processing speed were unchanged from immediate to 6 months postintervention, but group differences on an attention measure were not maintained
de Ruiter *et al*. (2016)	82 pediatric cancer survivors ages 8-18 years	Neurofeedback interventions: a total of 30 sessions, 30-min per session, twice per week, delivered at home or school	Attention, processing speed, memory, executive functioning, visuomotor integration, and intelligence	Subjects in both groups had similar improvements over time on the primary outcomes (all *P*s>0.05)
Hardy *et al*. (2013)	20 childhood cancer survivors of a brain tumor or ALL ages 8-16 years	Computerized working memory training program: a total of 25 training sessions at home, one session per week, delivered by phone-based coaching support	Performance-based and parent-report measures of working memory and attention	Subjects in the intervention program reported significant posttraining improvements in their visual working memory and parent-rated learning problems compared to those in the active control group
Hocking *et al*. (2019)	27 pediatric brain tumor survivors ages 7-16 years	Computerized working memory training: a total of 25 computer sessions delivered over 5-6 weeks. Each session lasted 30-45 min, including various aspects of working memory	Spatial span, digit span, and letter-number sequencing subtests from WISC, processing speed index, BRIEF, and the Child Behavior Checklist	This study did not find cognitive gains in pediatric brain tumor survivors with cognitive deficits by computerized working memory training
Mendoza *et al*. (2019)	68 childhood cancer survivors with a brain tumor or ALL ages 8-16 years	Computerized training: a total of 25 at-home training sessions over 5-9 weeks, each session lasted 30-45 min and included eight visual-spatial and verbal working memory games	Age-standardized abbreviated IQ test; working memory measures included WISC-IV spatial span, digit span, and letter-number sequencing tasks; and executive functioning by CPRS-3	Subjects in the intervention group reported cognitive gains but had no gains in social functioning
Moore *et al*. (2012)	57 pediatric cancer survivors with ALL ages <10 years	Mathematics intervention: a total of 40-50 h, delivered individually, and 1-2 h/week	WASI; processing speed index; verbal and nonverbal working memory; visual-motor integration skills, and fine motor speed and dexterity	Subjects in the intervention group reported significant improvements in mathematics at postintervention (*P*<0.05) and in visual working memory from baseline to 1-year follow-up (*P*=0.02)

BRIEF=Behavior Rating Inventory of Executive Function, CPRS-3=Conners' Parent Rating Scale-3, ES=effect size, WASI=Wechsler Abbreviated Scale of Intelligence

postintervention and 3/6-month follow-up. Six RCTs compared the academic/intellectual outcomes for pediatric cancer survivors, with a WMD of 3.36 (95% CI, 3.09–3.64; Figure 6a), and there were five trials involving 391 subjects that examined the effects of study interventions on academic/intellectual outcomes, with a WMD of 1.67 (95% CI, 1.40–1.94; Figure 6b). None of the studies reported adverse events related to neurocognitive and educational interventions.

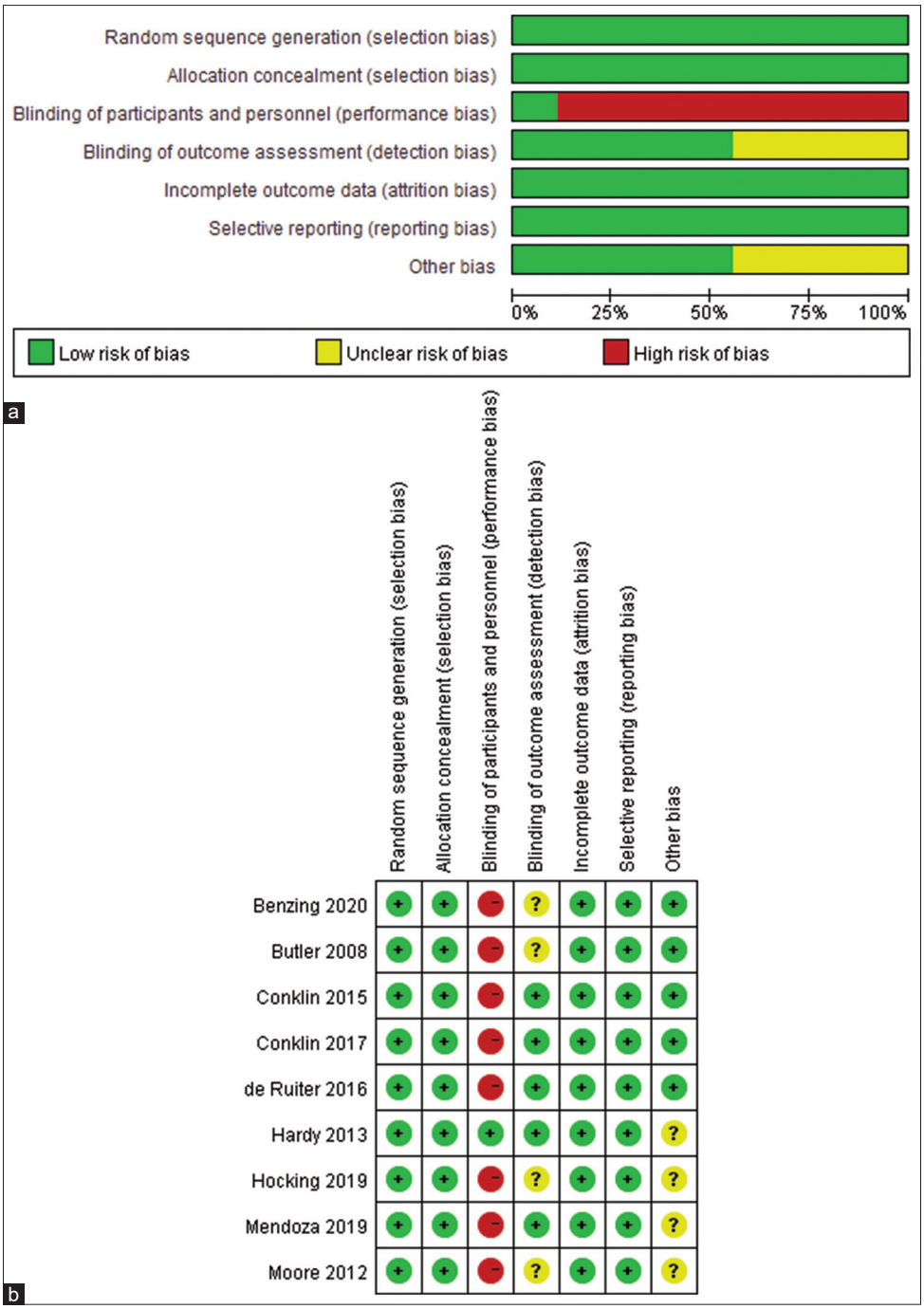

Figure 2: (a) Summary of risk of bias assessment. (b) Risk of bias assessment of each RCT

DISCUSSION

This meta-analysis summarizes direct comparisons of the effects of neurocognitive rehabilitation interventions on objective cognition and intellectual outcomes for pediatric cancer survivors. Neurocognitive rehabilitation consists of cognitive remediation, compensation, and education components.[2] The pooled intervention effect size ranged from 0.81 to 3.86 postintervention. The age range of pediatric cancer survivors in this study was 6 to 18 years. During this critical stage of brain development, any insult from central nervous system lesions or toxic agents, such as chemotherapy, to the developmental neural networks of the brain would have a more severe and dynamic effect on the pediatric brain than it would on the brain of an adult cancer survivor.[26]

A previous review summarized all possible interventions for cognitive dysfunction in pediatric cancer survivors.[2] This meta-analysis provides additional quantitative evidence on the effects of neurocognitive rehabilitation interventions in managing the cognitive outcomes of pediatric cancer survivors. As indicated by Hocking *et al.*,[23] cognitive remediation with

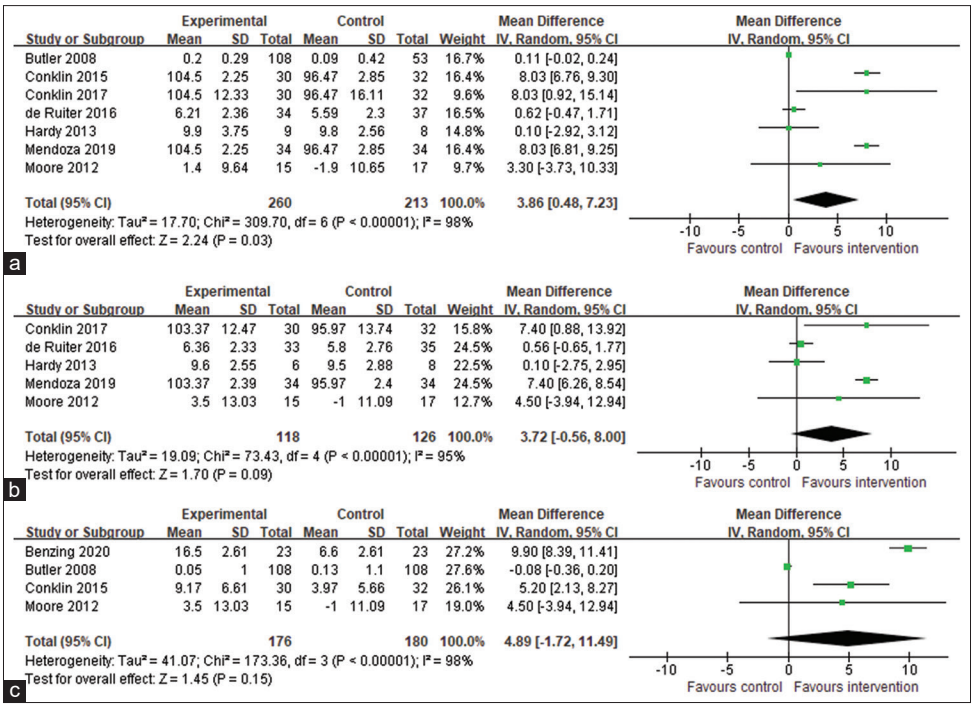

Figure 3: (a) Working memory at postintervention assessment. (b) Working memory at 3/6-month follow-up assessment. (c) Change in working memory from postintervention to follow-up assessment

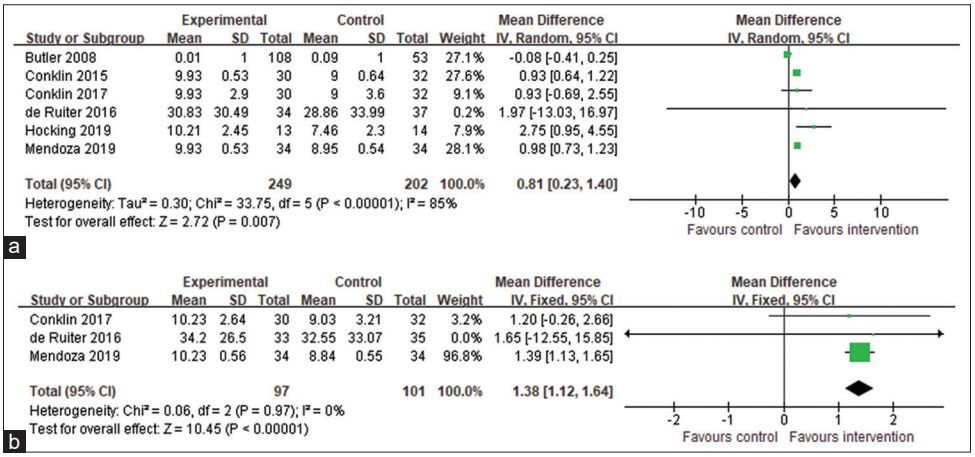

Figure 4: (a) Attention at postintervention assessment. (b) Attention at 3/6-month follow-up assessment

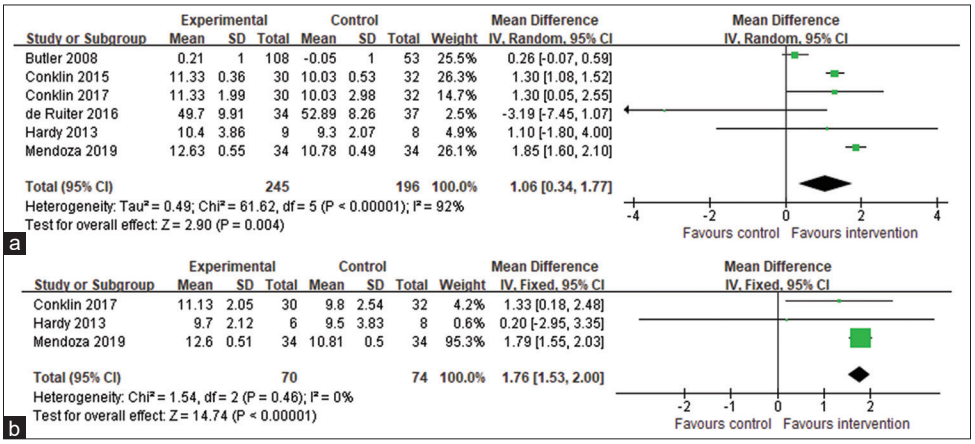

Figure 5: (a) Executive functioning at postintervention assessment. (b) Executive functioning at 3/6-month follow-up assessment

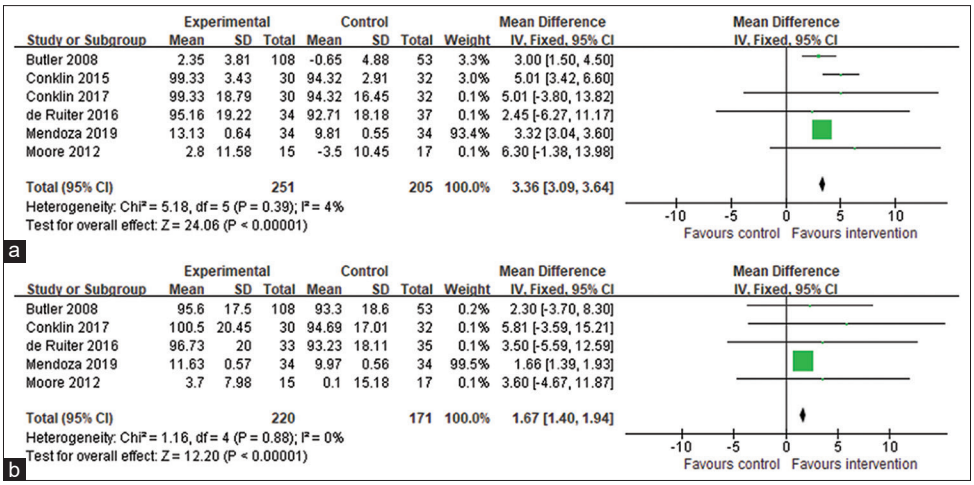

Figure 6: (a) Academic/intellectual performance at postintervention assessment. (b) Academic/intellectual performance at 3/6-month follow-up assessment

pediatric cancer survivors is a burgeoning area, and innovative intervention approaches are needed to enhance pediatric cancer survivors' cognitive outcomes. Indeed, technology-enabled interventions would increase their accessibility to cancer survivors.[27] A recent review recommended integrating machine learning and blockchain technologies into cancer care.[28] Hopefully, future research can apply these two most promising technologies to cognitive dysfunction management for pediatric cancer survivors, as globally there is an obvious trend of incorporating cutting-edge technologies into cancer care.

Although neurocognitive rehabilitation had positive effects on cognitive and intellectual outcomes in pediatric cancer survivors, the rehabilitation mechanism is largely unknown. Kesler *et al.*[13] conducted a single-arm trial of a cognitive rehabilitation program with pediatric cancer survivors and explored the possible intervention mechanism of this program on the cognitive dysfunction of this study population. This study suggested a possible rehabilitation mechanism that changes functional brain networks and enhances functional brain connectivity.[13] Some intervention research on adult cancer survivors also confirmed this possible rehabilitation mechanism.[29,30] Van der Gucht *et al.*[31] examined the effects of a mindfulness intervention on cancer-related cognitive impairment and explored the potential mechanism in adult survivors of breast cancer. They found that a mindfulness intervention has positive effects in terms of improving the cognitive functioning of adult cancer survivors and possibly enhancing the functional connectivity between dorsal and salience attention networks. Therefore, more research is required to explore the possible mechanisms of neurocognitive interventions in managing cognitive dysfunction and develop precision intervention strategies for ameliorating cognitive dysfunction among pediatric cancer survivors.

The limitations of this meta-analysis should be considered. The sample sizes in most RCTs in the meta-analysis were relatively small (20–161 subjects), thus limiting the generalizability of the findings. Most of the nine included trials conducted a short-term follow-up assessment of cognitive and intellectual outcomes. Hence, the long-term effects of neurocognitive rehabilitation interventions on pediatric cancer survivors are largely unknown. This, in part, may be due to practical issues, including limited available resources and a limited time frame for conducting the original study. Yet, future research should explore long-term changes among pediatric patients as a result of neurocognitive rehabilitation interventions for cognitive dysfunction.

CONCLUSION

This meta-analysis found that neurocognitive rehabilitation interventions improve the working memory, attention, and executive functioning of pediatric cancer survivors at postintervention and short-term follow-up. Neurocognitive rehabilitation also has positive effects on this study population's academic/intellectual performance during a vulnerable period in their development. Future research assessing long-term outcomes and employing larger sample sizes could confirm these positive effects of neurocognitive interventions for pediatric cancer survivors.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. American Child Cancer Organization. Childhood Cancer Statistics. Available from: https://www.acco.org/childhood-cancer-statistics/. [Last accessed on 2021 Nov 01].
2. Krull KR, Hardy KK, Kahalley LS, Schuitema I, Kesler SR. Neurocognitive outcomes and interventions in long-term survivors of childhood cancer. J Clin Oncol 2018;36:2181-9.
3. Zhi X, Xie M, Zeng Y, Liu JE, Cheng ASK. Effects of exercise intervention on quality of life in adolescent and young adult

cancer patients and survivors: A meta-analysis. Integr Cancer Ther 2019;18:1534735419895590.

4. Dutta V. Chemotherapy, neurotoxicity, and cognitive changes in breast cancer. J Cancer Res Ther 2011;7:264-9.
5. Dutta V. Psychostimulants for chemotherapy induced cognitive changes in cancer, Ockham's razor, anyone? J Cancer Res Ther 2012;8:326-9.
6. Riggs L, Piscione J, Laughlin S, Cunningham T, Timmons BW, Courneya KS, *et al.* Exercise training for neural recovery in a restricted sample of pediatric brain tumor survivors: A controlled clinical trial with crossover of training versus no training. Neuro Oncol 2017;19:440-50.
7. Phillips SM, Padgett LS, Leisenring WM, Stratton KK, Bishop K, Krull KR, *et al.* Survivors of childhood cancer in the United States: Prevalence and burden of morbidity. Cancer Epidemiol Biomarkers Prev 2015;24:653-63.
8. Castellino SM, Tooze JA, Flowers L, Hill DF, McMullen KP, Shaw EG, *et al.* Toxicity and efficacy of the acetylcholinesterase (AChe) inhibitor donepezil in childhood brain tumor survivors: A pilot study. Pediatr Blood Cancer 2012;59:540-7.
9. Mohrmann C, Henry J, Hauff M, Hayashi RJ. Neurocognitive outcomes and school performance in solid tumor cancer survivors lacking therapy to the central nervous system. J Pers Med 2015;5:83-90.
10. Hardy KK, Willard VW, Allen TM, Bonner MJ. Working memory training in survivors of pediatric cancer: A randomized pilot study. Psychooncology 2013;22:1856-65.
11. Conklin HM, Ogg RJ, Ashford JM, Scoggins MA, Zou P, Clark KN, *et al.* Computerized cognitive training for amelioration of cognitive late effects among childhood cancer survivors: A randomized controlled trial. J Clin Oncol 2015;33:3894-902.
12. Conklin HM, Ashford JM, Clark KN, Martin-Elbahesh K, Hardy KK, Merchant TE, *et al.* Long-term efficacy of computerized cognitive training among survivors of childhood cancer: A single-blind randomized controlled trial. J Pediatr Psychol 2017;42:220-31.
13. Kesler SR, Lacayo NJ, Jo B. A pilot study of an online cognitive rehabilitation program for executive function skills in children with cancer-related brain injury. Brain Inj 2011;25:101-12.
14. Mavrea K, Efthymiou V, Katsibardi K, Tsarouhas K, Kanaka-Gantenbein C, Spandidos DA, *et al.* Cognitive function of children and adolescent survivors of acute lymphoblastic leukemia: A meta-analysis. Oncol Lett 2021;21:262.
15. Review Manager (RevMan) [Computer program]. Version 5.4. The Cochrane Collaboration; 2020.
16. Drahota A, Beller E. RevMan Calculator. Available from: https://training.cochrane.org/resource/entering-data-revman-calculator.
17. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, *et al.*, editors. Cochrane Handbook for Systematic Reviews of Interventions. Version 6.2. Cochrane; 2021. Available from: www.training.cochrane.org/handbook. [updated February 2021].
18. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al.* The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021;372:n71.
19. Cox LE, Ashford JM, Clark KN, Martin-Elbahesh K, Hardy KK, Merchant TE, *et al.* Feasibility and acceptability of a remotely administered computerized intervention to address cognitive late effects among childhood cancer survivors. Neurooncol Pract 2015;2:78-87.
20. Benzing V, Spitzhüttl J, Siegwart V, Schmid J, Grotzer M, Heinks T, *et al.* Effects of cognitive training and exergaming in pediatric cancer survivors-a randomized clinical trial. Med Sci Sports Exerc 2020;52:2293-302.
21. Butler RW, Copeland DR, Fairclough DL, Mulhern RK, Katz ER, Kazak AE, *et al.* A multicenter, randomized clinical trial of a cognitive remediation program for childhood survivors of a pediatric malignancy. J Consult Clin Psychol 2008;76:367-78.
22. de Ruiter MA, Oosterlaan J, Schouten-van Meeteren AY, Maurice-Stam H, van Vuurden DG, Gidding C, *et al.* Neurofeedback ineffective in paediatric brain tumour survivors: Results of a double-blind randomised placebo-controlled trial. Eur J Cancer 2016;64:62-73.
23. Hocking MC, Paltin I, Quast LF, Barakat LP. Acceptability and feasibility in a pilot randomized clinical trial of computerized working memory training and parental problem-solving training with pediatric brain tumor survivors. J Pediatr Psychol 2019;44:669-78.
24. Mendoza LK, Ashford JM, Willard VW, Clark KN, Martin-Elbahesh K, Hardy KK, *et al.* Social functioning of childhood cancer survivors after computerized cognitive training: A randomized controlled trial. Children (Basel) 2019;6:105.
25. Moore IM, Hockenberry MJ, Anhalt C, McCarthy K, Krull KR. Mathematics intervention for prevention of neurocognitive deficits in childhood leukemia. Pediatr Blood Cancer 2012;59:278-84.
26. Rey-Casserly C, Meadows ME. Developmental perspectives on optimizing educational and vocational outcomes in child and adult survivors of cancer. Dev Disabil Res Rev 2008;14:243-50.
27. Fernandes HA, Richard NM, Edelstein K. Cognitive rehabilitation for cancer-related cognitive dysfunction: A systematic review. Support Care Cancer 2019;27:3253-79.
28. Cheng AS, Guan Q, Su Y, Zhou P, Zeng Y. Integration of machine learning and blockchain technology in the healthcare field: A literature review and implications for cancer care. Asia Pac J Oncol Nurs 2021;8:720-4.
29. Revannasiddaiah S, Gupta M, Seam R, Gupta M. The neurobiological basis of anti-cancer therapy induced cognitive dysfunction and the promising pharmacological modalities against the same. J Cancer Res Ther 2012;8:162-3.
30. Dutta V. Uncomfortable bedfellows: Whole brain radiation therapy and neurocognition in animal and human studies. J Cancer Res Ther 2015;11:679-83.
31. Van der Gucht K, Ahmadoun S, Melis M, de Cloe E, Sleurs C, Radwan A, *et al.* Effects of a mindfulness-based intervention on cancer-related cognitive impairment: Results of a randomized controlled functional magnetic resonance imaging pilot study. Cancer 2020;126:4246-55.

APPENDIX 1 SEARCH STRATEGY IN DATABASES

PUBMED/EMBASE/SCOPUS/PSYCHINFO search strategy

1. exp Neoplasms/or exp Bone Marrow Diseases/or exp Bone Marrow Transplantation/or exp Stem Cell Transplantation/or exp Radiotherapy/or exp Chemotherapy, Adjuvant/or exp Antineoplastic Combined Chemotherapy Protocols/or exp Salvage Therapy/or exp Palliative care/
2. (neoplasms* or cancer* or tumour* or tumor* or malignan* or carcino* or lymphoma* or adenocarcinoma* or radioth* or radiat* or irradiat* or radiochemo* or chemotherap* or (bone adj marrow adj5 transplant*)).mp.
3. 1 or 2
4. exp cognitive impairment
5. (cognitive dysfunction* or "cognition disorders"[Mesh]) or cognition disorders)).mp.
6. 4 or 5
7. exp psychology, social/or exp psychotherapy
8. (psychosocial$ or psycho-social$).mp.
9. (counsel$ or (behaviour$ adj4 therap$) or "training" or (behavior$ adj4 therap$) or (relax$ adj4 therap$) or (relax$ adj4 treatment$) or (support$ adj4 group$) or imagery or "energy conservation" or "stress management" or psychotherapy$ or "self-care" or "self-help" or biofeedback or educati$ or psychoeducat$ or relaxation therap$ or "nursing intervention" or "nursing support").mp.
10. 17. or 7-9 (*Psychosocial Interventions*)
11. Randomized controlled trial.pt.
12. controlled clinical trial.pt.
13. pediatric*
14. childhood
15. or 11-14.