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Original Article

Preliminary Near-Transfer Effects of a Manualized Cognitive Training Toolkit for Pediatric Cancer Survivors: A Nonrandomized Feasibility Trial

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Abstract

Introduction Computerized cognitive training has reasonable evidence for ameliorating cognitive deficits in childhood cancer survivors; however, availability, affordability, and nonadaptation are impending factors. Despite therapist-delivered cognitive training has similar effects, there is no indigenous and replicable structured manualized cognitive training for childhood cancer survivors in India.

Objective The feasibility and indicative impact assessment of a manualized cognitive training toolkit (MCTT) (similar effect size as CogMed working memory training and PSSCogRehb software for children with attention deficit hyperactivity disorder) was examined to fabricate to meet the needs of the target group.

Materials and Methods With a pre–post design, 10 survivors (M = 8, F = 2) between 6 and 11 years (mean age = 8.6 ± 2.7 years) with Social Quotient (SQ) $\geq$ 85 (mean SQ = 99.8 ± 11.75), and having significant cognitive deficits were recruited. Far-transfer effects were assessed through parents' rated Child Behavior Rating Scale, and near-transfer effects through Cognitive Assessment System-2.

Results Note that 58.33% had cognitive deficits across planning, attention, and successive and simultaneous processing. MCTT with 18 cognitive tasks (16 difficulty levels) delivered in 8 days (over 2 weeks:16 hours) was feasible. Except attention domain, MCTT had significant near-transfer effects on planning ($Z = 2.88$, $p < 0.01$, $r = 0.86$), simultaneous ($Z = 2.55$, $p < 0.01$, $r = 0.81$), and successive processing ($Z = 2.45$, $p < 0.01$, $r = 0.77$) with large effect size.

Discussion MCTT was a feasible toolkit; however, refabrication with increased number of attention-focused tasks and difficulty levels was indicated. Expectedly, MCTT did not have positive/negative impacts on behaviors.

Conclusion MCTT has potentiality for a randomized controlled trial and can be compared to any computerized training for this target group.

Keywords
- MCTT
- pediatric cancer survivors
- cognitive deficits

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Introduction

Cancer and its intensive treatment occurring at a critical period of child development result in difficulty in "thinking, information processing, and remembering," often known as late effects occurring even after a decade of treatment.[1] This can substantially disrupt the development of normal cognitive progression and negatively affect higher-order mental processes such as attention, visuospatial skills, learning and language, and executive functioning including working memory, sequencing, and processing speed of the survivors.[2,3] Also, information processing speed could be affected due to the impact of neurotoxin on white matter,[4] ultimately affecting intellectual functioning.[5–8]

The prevalence of cognitive deficits varies, affecting 15 to 75% of survivors,[9–11] and as high as 50 to 80% among pediatric brain tumor survivors.[12] A retrospective clinical review revealed that within a year of treatment 51.9% showed deficits in processing speed while 41.4% exhibited deficits in working memory.[13] Another study reported requirement of additional resources for 28% of survivors.[14]

Early identification and amelioration of cognitive deficits are essential. Therefore, development of cognitive training/rehabilitation plays a pivotal role in elevating the level of core cognitive functioning.[15] Although pharmacological treatment has been found effective in reducing attention deficits, the treatment reachability remains limited due to parental reluctance, endocrinopathies, seizures, risk of interaction with current medications, or risk of side effects.[16] In contrast, there is reasonable evidence for positive effects of various neurocognitive interventions in improving the cognitive functioning and academic achievement of the survivors.[17–20]

The therapist-delivered cognitive and problem-solving intervention demonstrated improved meta-cognitive skills and academic performance among childhood cancer survivors. Subsequently, as an alternative viable option with no side effects, the computerized cognitive intervention programs appeared promising and future-oriented for improving multiple neurocognitive domains instead of only one attention domain.[16,21–25] Computerized training (Captain Log—a home-based 12-week cognitive training program) improved working memory and reduced parents' rated attention in pediatric cancer survivors even after 3 months. In a meta-analysis of nine intervention studies, reported that neurocognitive rehabilitation yielded significant improvements in working memory, along with continued gains observed 3–6 months after the intervention in areas of attention, executive function, and academic or intellectual performance.[26] Thus, studies on computerized training (e.g. Captain-Log and COGMED working memory training) reported near-transfer effects (improvement on the trained tasks) for survivors.

However, computerized training may not be plausible for a resource-limited country like India, due to a myriad of reasons including high cost, custom-related difficulty, license/limited time subscription issues, language incompatibility, meeting the level of task difficulty, and lack of cultural competency of tasks. Due to substantial absence from school or lack of exposure to the reading ability language competency of Indian pediatric cancer survivors are low. This makes few tasks unsuitable, for example, verbal or language-based tasks in the computerized interventions that might notably affect survivors' performance. Low socioeconomic status is also a big hindrance for their exposure to computer desktop/laptop, hence speed and accuracy on tasks. Further, survivors' follow-up is generally done in the survivors' clinic at the outpatient departments (OPDs) of cancer hospitals in India, which mostly are not equipped with computer desktops to apply computerized interventions. Also, the availability of desktops/laptops with the parents/families for implementing home-based/Internet-based computerized cognitive training is questionable for Indian survivors. In this context, it would be worth exploring the impact of an indigenous, structured, and largely culture-free noncomputerized/manualized cognitive training targeting planning, memory, and processing speed-related deficits in pediatric survivors. Again, the existence and impact of therapist-delivered manualized cognitive intervention in reducing cognitive deficits have been reported in the literature[20]; however, their replicability is not reported. Additionally, till date only one interventional study was published by Patel et al, in 2009,[20] however, it lacked a structured and replicable format. Also, it was not tested on survivors exhibiting definite cognitive deficits on standard tools. Further, so far, no therapist-delivered/manualized cognitive training examined their far-transfer effects on behavioral problems.

This study examined the feasibility and indicative near- and far-transfer effects of a structured manualized cognitive training toolkit (MCTT)[27,28] for pediatric cancer survivors with cognitive deficits.

Materials and Methods

Study Design

The study was an exploratory research and a pre–post design was adopted to test the feasibility and indicative effect of the MCTT. Referrals of children registered at the survivor's clinic of the oncology department and the oncology division of the pediatrics department of a tertiary care hospital were screened for inclusion.

Participants

►**Fig. 1** presents the sample recruitment flowchart. A total number of 38 pediatric cancer survivors were enrolled in the study and the preassessment was carried out. Out of these, $n = 26$ were excluded either due to absence of cognitive deficits or dropout due to logistic and financial reasons. So, $n = 12$ patients were included for intervention but 2 patients further dropped out after initial few sessions and the final sample consisted of $n = 10$ childhood cancer survivors who completed all sessions of the intervention protocol.

Inclusion Criteria

Male and female pediatric cancer survivors aged 6 to 11 years, Social Quotient (SQ) $\geq$ 85 on the Vineland Social Maturity Scale (VSMS), and had significant cognitive deficits on the Cognitive Assessment System-2 (CAS-2) were eligible.

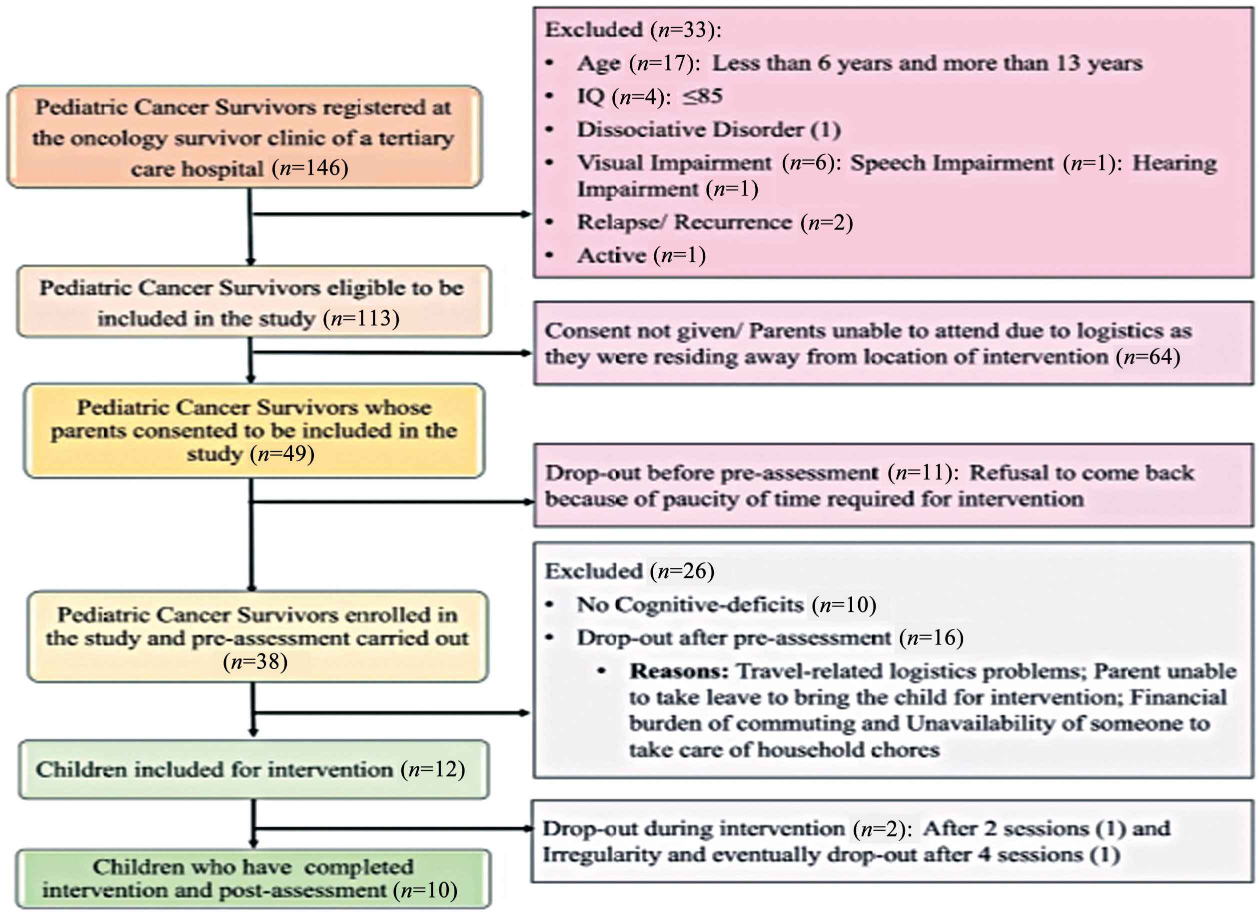

Fig. 1 Recruitment flowchart ($n = 10$).

Exclusion Criteria

Survivors were excluded if they had preexisting medically diagnosed psychiatric disorders or neurodevelopmental (attention deficit hyperactivity disorder [ADHD], autism, specific learning disorder) or congenital conditions (Down syndrome, fragile X syndrome, global developmental delay, WAGR syndrome), children who had undergone brain surgery as a part of their cancer treatment regimen, and physical disabilities (visual, hearing, and upper extremity).

Expected Outcomes

Primary Outcomes

Primary outcomes are the near-transfer effects of the MCTT for pediatric cancer survivors assessed using CAS-2.

Secondary Outcomes

Secondary outcomes are the possibility of behavioral issues among pediatric cancer survivors.

Assessment Tools

Vineland Social Maturity Scale

The social maturity and adaptive behavior was assessed through the VSMS,[29,30] with 89 items across 5 domains: communication, daily living skills, socialization, motor abilities, and self-help skills. Intelligence quotient/SQ screening was done on the basis of VSMS as per the Indian Disability Gazette of 2024.

Cognitive Assessment System-2

The neurocognitive functioning was assessed through the CAS-2[31] across PASS domains (Planning, Attention, Simultaneous processing, and Successive processing). Out of 12 subtests, 8 were used for assessing children's strengths and cognitive deficits.

Child Behavior Checklist

Parents' rated Child Behavior Checklist (CBCL) by Achenbach[32] was used to assess child's behavior.

Intervention Description

Manualized Cognitive Training Toolkit

The MCTT[27,28] grounded in PASS theory, is a structured, multidomain therapists-delivered intervention that is administered in one-on-one format. It features 36 cognitive activities, spanning over 9 domains: planning, sustained attention, simultaneous processing, successive processing, working memory, language skills (one task of education standard-1 level), visual-spatial processing, and mind-motor coordination. Each task has eight difficulty levels, each consisting of two sessions. To achieve a basic competency level, a child has to pass the four difficulty levels (8 sessions). MCTT was designed to target children aged 6 to 11 years with ADHD and demonstrated similar or better effects than computerized tools (e.g., COGMED and PSSCog-Rehab). It had no far-transfer effects for children with ADHD.

MCTT in our study was carried out in a designated room in a hospital OPD setup. Parents were allowed to witness the activities. The survivors were given a break in between to curb the fatigue effect. The intervention fidelity was maintained as all the therapists were trained in carrying out MCTT in a past study.

Ethical Approval

Ethics clearance was obtained from an institutional ethics body of a large public sector medical college vide IEC-82/04.02.2022, RP-18/2022, OP-10/15.06.2023. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Results

Cognitive profiling and behavioral problem screening were conducted for 38 pediatric cancer survivors. Out of this, 10 children who scored average and above on the full-scale of CAS-2 for no cognitive deficits and 16 children after baseline assessment who did not provide consent were excluded. Finally, 10 (male = 8, female = 2) participants aged 6 to 11 years (mean = 8.6 years, standard deviation [SD] = 2.70) with SQ $\geq$ 85, IQ range = 91–127, mean SQ = 99.8, SD = 11.75) completed this pilot study. Of the 10 participants, 6 (60%) had rejoined school following the completion of treatment (one each in class UKG, 2, 3, and 5, and two in nursery); however, 4 (40%) of them had not yet resumed formal education.

The participants had a diagnosis of Wilms' tumor ($n = 3$, 30%), retinoblastoma ($n = 2$, 20%), neuroblastoma ($n = 1$, 10%), hepatoblastoma ($n = 1$, 10%), brain tumor ($n = 1$, 10%), Hodgkin's lymphoma ($n = 1$, 10%), and synovial sarcoma ($n = 1$, 10%). The mean duration of the survivorship phase among participants was 2.19 years, with a range spanning from 2 to 96 months. Mean age of onset of illness was 3.7 years.

The gap between baseline and first intervention session was 1 to 2 days and postintervention assessment was done on the next day of intervention completion, except in one case where it was done on the same day of last intervention session. We did not analyze the intention to treat children ($n = 2$) to strictly look into the impact and feasibility issues so as to make the MCTT new intervention protocol most appropriate for cancer survivors.

Preliminary Impact Assessment

►**Table 1** revealed that approximately 30 to 66% of these children experienced cognitive deficits in areas such as planning, attention, and successive and simultaneous processing. Additionally, 58.33% had overall cognitive impairments across these four domains.

►**Table 1** revealed that MCTT demonstrated exceptional ability to reduce cognitive deficits in full-scale domains of CAS-2. While all 10 children had cognitive functioning in the below average–very poor range, MCTT intervention for 16 intensive hours could convert scores of six children (60%) into average and above average scores for cancer survivors. A total of nine children were able to reduce their cognitive deficits and 30 to 60% of children had changed scaled scores on successive processing, simultaneous processing, planning, and attention domains. This was corroborated when the mean pre–post intervention scores on all domains were compared in ►**Table 2**, which indicated that there were significant mean differences on planning, simultaneous, and successive processing along with the full-scale CAS-2. The effect size of the mean score difference was large for all these three domains and the full scale although the

Table 1 Pre–post percentage change in CAS-2 scores

Pre–post comparison of percentage of change in CAS-2 scores						
Planning						
Interpretation	**Index score**	**Pre**		**Post**		**Percentage change**
		f **(%)**	**Combined** ***f*** **(combined%)**	***f*** **%**	**Combined** ***f*** **(combined%)**	
Very poor	< 70	3 (30)	9 (90)	1 (10)	5 (50)	40
Poor	70–79	2 (20)		1 (10)		
Below average	80–89	4 (40)		3 (30)		
Average	90–109	1 (10)	1 (10)	4 (40)	4 (40)	30
Above average	110–119	0 (0)	0 (0)	1 (10)	1 (10)	10
Superior	120–129	0 (0)		0 (0)		
Very superior	> 130	0 (0)		0 (0)		

Table 1 (*Continued*)

Pre–post comparison of percentage of change in CAS-2 scores						
Planning						
Interpretation	**Index score**	**Pre**		**Post**		**Percentage change**
		f **(%)**	**Combined** ***f*** **(combined%)**	***f*** **%**	**Combined** ***f*** **(combined%)**	
Simultaneous						
Interpretation	**Index score**	**Pre**		**Post**		**Percentage change**
		f **(%)**	**Combined** ***f*** **(combined %)**	***f*** **(%)**	**Combined** ***f*** **(combined %)**	
Very poor	< 70	1 (10)	6 (60)	0 (0)	0 (0)	60
Poor	70–79	2 (20)		0 (0)		
Below average	80–89	3 (30)		0 (0)		
Average	90–109	4 (40)	4 (40)	8 (80)	8 (80)	40
Above average	110–119	0 (0)	0 (0)	2 (20)	2 (20)	20
Superior	120–129	0 (0)		0 (0)		
Very superior	> 130	0 (0)		0 (0)		
Attention						
Interpretation	**Index score**	**Pre**		**Post**		**Percentage change**
		f **(%)**	**Combined** ***f*** **(combined%)**	***f*** **(%)**	**Combined** ***f*** **(combined%)**	
Very poor	< 70	0 (00)	8 (80)	1 (10)	5 (50)	30
Poor	70–79	5 (50)		1 (10)		
Below average	80–89	3 (30)		3 (30)		
Average	90–109	2 (20)	2 (20)	4 (40)	4 (40)	20
Above average	110–119	0 (0)	0 (0)	0 (0)	1 (10)	10
Superior	120–129	0 (0)		1 (10)		
Very superior	> 130	0 (0)		0 (0)		
Successive						
Interpretation	**Index score**	**Pre**		**Post**		**Percentage change**
		f **(%)**	**Combined** ***f*** **(combined %)**	***f*** **(%)**	**Combined** ***f*** **(combined %)**	
Very poor	< 70	0 (0)	4 (40)	0 (0)	1 (10)	30
Poor	70–79	2 (20)		1 (10)		
Below average	80–89	2 (20)		0 (0)		
Average	90–109	6 (60)	6 (60)	7 (70)	7 (70)	10
Above average	110–119	0 (0)	0 (0)	2 (20)	2 (20)	20
Superior	120–129	0 (0)		0 (0)		
Very superior	> 130	0 (0)		0 (0)		
Full scale						
Interpretation	**Index score**	**Pre**		**Post**		**Percentage change**
		f **(%)**	**Combined** ***f*** **(combined %)**	***f*** **(%)**	**Combined** ***f*** **(combined %)**	
Very poor	< 70	2 (20)	10 (100)	0 (0)	4 (40)	60
Poor	70–79	1 (10)		1 (10)		
Below average	80–89	7 (70)		3 (30)		
Average	90–109	0 (0)	0 (0)	5 (50)	5 (50)	50

(*Continued*)

Table 1 (*Continued*)

Pre–post comparison of percentage of change in CAS-2 scores						
Planning						
Interpretation	**Index score**	**Pre**		**Post**		**Percentage change**
		f **(%)**	**Combined** ***f*** **(combined%)**	***f*** **%**	**Combined** ***f*** **(combined%)**	
Above average	110–119	0 (0)	0 (0)	1 (10)	1 (10)	10
Superior	120–129	0 (0)		0 (0)		
Very superior	> 130	0 (0)		0 (0)		

Abbreviation: CAS-2, Cognitive Assessment System-2.

Table 2 Wilcoxon signed-rank analysis of planning, simultaneous, attention, successive, and full-scale index scores on CAS-2

Index scores	Preintervention scores ($n = 10$)		Postintervention scores ($n = 10$)		Z	r	Percentage of change (%)
	Median	Mean ± SD	Median	Mean ± SD			
Planning	78	75.9 ± 9.89	89.5	90.3 ± 13.06	2.80[b]	0.885 L	18.97
Simultaneous	86.5	84.5 ± 12.92	100	100 ± 8.73	−2.55[b]	−0.806 L	18.34
Attention	80.5	82.4 ± 6.90	91	89.9 ± 14.95	−1.43	−0.452	9.10
Successive	92.5	93.9 ± 13.17	97	99.5 ± 13.30	−2.45[a]	−0.774 L	5.96
Full scale	81	79.5 ± 8.07	96	94.5 ± 10.39	−2.80[b]	−0.885 L	18.87

Abbreviations: CAS-2, Cognitive Assessment System-2; SD, standard deviation.
[a] $p < 0.05$.
[b] $p < 0.01$.

Table 3 Subtest pre–post comparison

Domain	Subtest scaled scores	Preintervention scores ($n = 10$)		Postintervention scores ($n = 10$)		Z	r	% of change
		Median	Mean ± SD	Median	Mean ± SD			
Planning	Planned code	6.5	6.3 ± 1.85	8	8.3 ± 2.57	−2.50**	−0.791 L	31.75
	Planned connection	7	5.7 ± 1.95	9	8.5 ± 2.69	−2.67**	−0.844 L	49.12
Simultaneous	Matrices	8	8.1 ± 3.28	10	10.6 ± 2.55	−1.99*	−0.629 M	30.86
	Verbal spatial relations	6.5	6.6 ± 2.46	10	9.5 ± 1.84	−2.67**	−0.844 L	43.94
Attention	Number detection	5.5	6.2 ± 3.19	6.5	7 ± 3.59	−0.46	−0.145	12.90
	Expressive attention	9	8.5 ± 1.43	9	9.7 ± 2.41	−1.61*	−0.509 M	14.12
Successive	Word series	10	9.9 ± 2.18	11	11.2 ± 3.12	−1.89*	−0.598 M	13.13
	Visual digit span	5.5	5 ± 4.85	5.5	5.1 ± 4.93	−0.31	−0.098	2

Abbreviation: SD, standard deviation.
Note:
*$p<0.05$
**$p<0.01$

percentage of change in scores ranged < 20%. The mean difference on attention domain was not significant despite ►**Table 1** and parents' rated attention deficits showed substantial changes in attention. ►**Table 3** expanded the findings of ►**Table 2** to indicate that MCTT had significantly improved cognitive functioning with large effect size on planned codes, planned connections, and visuospatial relationship; and medium effect size on matrices, expressive attention, and word series. The percentage of change observed was > 49 and 44%, respectively, for planned connections and verbal spatial relations, and > 30% for planned code and matrices.

Feasibility Analysis (►Table 4)

Of all the consented participants 77.55% were recruited and all of them completed baseline assessment. Out of the baseline assessed, 31.58% participated in the intervention and 83.33% completed the designated intervention MCTT; thus, a high retention rate was seen. While all survivors viewed the

Table 4 Feasibility evaluation of MCTT for pediatric cancer survivors

Domain of feasibility evaluation	Criteria of feasibility evaluation	Findings (frequency and %, wherever applicable)
Recruitment and eligibility	Number of potential participants eligible	113
	Number of children screened consented for intervention	49
	Number of children recruited	38 (77.55%)
Data collection on pre–post intervention assessment scales	% Completing baseline assessment	38 (100%)
	% included for intervention	12 (31.58%)
	% Completing post-assessment	10 (83.33%)
Attrition	Dropout rate	16.66%
	Retention rate	83.33%
	Average number of weeks sessions were conducted	2 weeks
	Average number of sessions conducted to work through the intervention	8 sessions
	Total session duration estimated	16 hours
	Average session duration	2 hours
Participants' adherence to intervention	Adherence to intervention	Average no. of planned sessions = 8 + 1 baseline and 1 post-assessment
		Average no. of conducted sessions = 8 + 1 baseline + 1 post-assessment
Status of completion of the MCTT original intervention for children with ADHD	Original no. of cognitive tasks = 36 Applied tasks = 35	Average no of completed tasks = 18 (50%) (MCTT Protocol of 18 activities attached as ►**Supplementary material**.)
	Original no. of cognitive domains = 9 Applied domains = 8 (excluding body balance domain)	No. of completed domains = 7 (language domain could not be completed by all due to low education level)
	Original no. of difficulty levels in each task 4	No of completed difficulty levels = 4 (all completed basic competency)
Response to intervention	Acceptance of intervention by the participants	10 (100%) Done through short 4-point Likert feedback form
	Number of participants with subjective rating of improvement	10 (100%)
	Objective assessment of improvement	9 (90%)

Abbreviations: ADHD, attention deficit hyperactivity disorder; MCTT, manualized cognitive training toolkit.
Note: Adapted from Orsmond and Cohn, 2015.

positive effect of MCTT, objectively 90% of survivors exhibited reduction in cognitive deficits and improvement in the full-scale CAS-2. Although MCTT met the five feasibility parameters of Orsmond and Cohn,[33] except the added criteria of completion of the entire MCTT by the authors. Only 50% of the planned cognitive tasks were completed in 16 hours of 8 days of intervention over a period of 2 weeks.

Behavioral Problems

None of the children received any significant scores on overall internalizing and externalizing behavior domains of the parents' rated CBCL either at baseline or immediate postintervention. However, two children were found to be attention deficits at a clinical level (baseline assessment) but at the immediate postintervention assessment, both scored at a normal range on attention and the mean scores of all survivors were similar on attention after MCTT.

Discussion

Neurocognitive training/rehabilitation through computerized and manualized interventions contain focused cognitive training tasks in one or multiple cognitive domains, with the goal of improving accuracy and speed[34] of the target groups on the trained tasks. Both formats intend to enhance a child's ability[35] to improve speed and accuracy on the trained task and thus, have the potential to lessen cognitive deficits.[36]

MCTT as a Structured Cognitive Intervention

In comparison to traditional therapist-led cognitive interventions[17,19,20], the MCTT demonstrated markedly higher compliance and feasibility. While earlier therapist-directed programs [17,19,20] yielded improvements in select neurocognitive domains, their implementation was often constrained by issues such as participant adherence, high resource demands, and the necessity of in-person sessions. Moreover, these interventions were generally not grounded in theoretical frameworks and lacked a structured, replicable design with cognitive tasks systematically organized by domain and graded difficulty. The MCTT[27,28], however, employs a theory-driven, standardized structure with clearly defined modules and four progressive difficulty levels across multiple cognitive domains, thereby improving both scalability and participant engagement. The replicability of MCTT across culture might be better than these cognitive interventions, as MCTT has 95% nonlanguage-based cognitive tasks. The tasks are designed to meet the cognitive development and capacity of the children aged 6 to 11 years. Tasks also target evidence-driven cognitive deficits found in pediatric cancer survivors, unlike computerized interventions which are generalized and not developed as per the cognitive age and specific deficits of survivors. In the absence of structured, largely culture-fare, and replicable therapist-delivered cognitive training, MCTT could be very useful for low-middle-income countries including India.

Sample Size

Two existing feasibility studies are published till date. The sample size of our study was better than the first cognitive intervention of cancer survivors with only one adolescent[37] and a feasibility study with three survivors.[38] However, our sample size ($n = 34$) is less than the feasibility study on Cogmed computerized training by Cox et al.[39] This could be attributed to survivors not staying in the close proximity of the hospital where survivors' follow-up is done, poor knowledge and nonpriority of parents on cognitive deficits and their long-term repercussion on survivors' quality of life, and no formal psychoeducation session and materials on the topic in survivors' clinic. Our sample size was similar (Patel et al, 2009 with 12 samples) and better than a pilot study on computerized training (CaptainLog) with 9 samples.[20,22]

Target Age

While survivors aged 8 to 16 years participated in Cox et al[39] and 9 to 14 years in van't Hooft and Norberg's[38] study, our sample aged between 6 and 11 years who belonged to the concrete operational stage of Piaget's cognitive/intelligence development theory. This could be the most appropriate age for cognitive intervention due to beginning of logical and organized thinking. Nevertheless, many pilot studies including randomized controlled trials (RCTs) have taken a wide age range (e.g., 7–19 years, Kesler et al,[25] Patel et al, 6–22 years,[20] Butler and Copeland, 6–17 years,[40] Butler et al, 10–17 years,[17] Hardy et al, 8–16 years,[22,23] and main study 8–16 years: Conklin et al[16]). As the cognitive development in humans is gradual, age-specific, and almost universal, targeting either preoperational stage (2–7 years, by this time majority of cancer patients do not reach the survivors' stage) or 6/7 to 11 years (evidence-based as many patients reach survivors' phase at this age), it is prudent to design cognitive interventions as per the cognitive ability, capacity, and flexibility of children in a particular age bracket.

Comparative Group

Cox et al study[39] was a methodologically stronger feasibility study as it had a wait list control. However, even a multicenter pilot study had 20 samples without a comparative group.[17] Our study was in line of earlier feasibility[38] and pilot study.[17–20]

Off-Medication/Duration of Survivorship

The mean duration of the survivorship was 2.19 years (1–6 years) in our study, which was different from almost all reported feasibility, pilot, and main studies mentioned earlier in which 1 year off therapy was prevalent.

Feedback/Acceptance

Our feedback questionnaire had seven questions each in the child and parent version to assess acceptance/satisfaction. It was not as robust as used by Cox et al[39] but was better than many studies which did not evaluate acceptance or feedback.

Preliminary Near-Transfer Impact Analysis of MCTT

MCTT had significantly reduced cognitive deficits with large effect size for planned code, planned connection, verbal, and spatial relations; medium effect size for matrices, expressive attention, and word series. Improvement in terms of 30 to $>$ 49% changes in scores of these six subscales was satisfactory and in line with other studies. There was no significant improvement on number detection, expressive attention, and visual digit span. Pediatric cancer survivors display a diverse set of neurocognitive deficits and since MCTT contained cognitive tasks in eight domains with four increasing difficulty levels and 18 activities/cognitive tasks Protocol attached as ►**Supplementary material** (available in Online only version), it benefited in reducing cognitive deficits as reflected in five domains. However, no significant improvement in attention index scores on CAS-2 could be due to the long survivorship, for example, up to 6 years, and MCTT should be customized to cater to specific needs of such survivors.

Feasibility Analysis of MCTT

MCTT met the five feasibility parameters,[33] except the added criteria of completion of the entire original MCTT by the authors. Although 77.55% of the consented participants were recruited and completed baseline assessment, only 31.58% participated in the intervention. This low conversion rate of consent to actual participation could be attributed to not following the staggered recruitment strictly as in a randomized trial,[41] patients not living in a geographical location proximity to the hospital where the services were provided, logistic issues, and parents' perception of cognitive dysfunction as a nonpriority issue. This is in line of studies reporting participation rates and adherence tend to be low, while time and financial costs are high for modest benefits in cognitive interventions of pediatric cancer survivors.[17,19,20]

Especially, we could not finish all 36 activities in the original MCTT and reduced 50% of cognitive tasks contained in the original MCTT because of many challenges: (1) To reduce the risk of attrition and to keep it less burdensome for the survivors as the motivation to seek treatment, adherence, and compliance were often fragile in children in developing countries.[42] (2) Pediatric cancer survivors have slow processing efficiency,[43] therefore, need more intervention time to complete all tasks for which parents were not willing. (3) Since majority of parents lived in different cities, bearing the logistics and financial burden of staying longer time at this hospital location for a nonpriority concern could increase dropout risk.

In this study, 83.33% completed the designated intervention MCTT, thus a high retention rate. The retention rate was similar to clinic-based cognitive training programs with completion rates of approximately 70 to 80% for children with ADHD.[44] Also, since participants and their parents were recruited from survivor's clinic during their follow-up visit, they were psychoeducated in details on the late effects of cancer treatment on cognitive functioning, risks and benefits of cognitive intervention, etc. Further discussion with parents guided us to know the maximum days they can stay to participate in the intervention. Therapists' rapport with the parents and children and eagerness of the participating parents to improve children's core cognitive deficits could have also contributed to the successful retention. Moreover, telephonic reminders for sessions, allowing parents in the session, and briefing them on child's performance, excel tracking sheet, could have facilitated the retention.[45] In summary, high adherence to and acceptability of interventions could be attributed to: (1) parents' psychoeducation, flexible time slots of intervention as per parents' conveniences, and consistent communication by the research team; (2) varieties of cognitive tasks perhaps kept the monotony and predictability of tasks intervention at bay, hence helped in sustained motivation of the survivors; (3) the performance feedback on various tasks perhaps provided a sense of competency to the children; and (4) participant's interest, engagement, involvement, and perceived benefits of the intervention and perception of interventions as not too technical or demanding. So, we can say that as a nonrandomized trial, refabricated MCTT was feasible and had positive effects on the neurocognitive functioning of the pediatric cancer survivors.

Limitations

Although, this feasibility study aimed to finalize the MCTT protocol for the pediatric cancer survivors to reduce cognitive deficits in shortest possible time, the preliminary near-transfer effects on the trained tasks were promising. A few limitations could have been addressed. Recruiting a control group could have been presented a better comparative finding. A direct comparison of MCTT with Cogmed or other computerized cognitive training programs could have strengthened the study's findings, as both approaches have demonstrated efficacy. Computer-assisted interventions have been shown to improve attention, working memory, and executive functioning while providing benefits in standardization, scalability, and replicability.[46] Similarly, a study by Rastogi et al[47] emphasizes the need for structured, theory-driven, and culturally adapted interventions for pediatric cancer survivors in India, which have also been shown to be effective and feasible, as exemplified by MCTT.[27,28] Also, a follow-up assessment after 1/3/6 months could have demonstrated the maintenance of benefits of MCTT.

Gray Areas

The following concerns could have reduced the dropout rate and possibly could have provided better results like recruitment of local survivors, regular psychoeducation of parents (prior to recruitment) with distribution of psychoeducation materials in local language in the survivors' clinics, and extended training days to cover the 36 cognitive tasks in the original MCTT.

Future Directions

Future studies can be planned where MCTT can be compared with other computerized training programs to see its efficacy in comparison of already existing computerized treatment programs. Further, intervention on a larger sample size will increase the power of the study.

Generalizability of the Study

Since the study had a small sample size, it did not have high generalizability at present but it can be tested with the same population using a larger sample size and a RCT. Further, having computerized treatment approaches as a comparative treatment modality will provide strength to the study.

Conclusion

MCTT with 50% of cognitive tasks (18 tasks with 4 difficulty levels) was found feasible for cancer survivors aged 6 to 11 years and improved index scores on domains of planning, simultaneous, and successive processing. Before attempting a randomized trial, it can be refabricated to include tasks from the original toolkit, focusing mainly on attention. Essential psychoeducation on "reduction of late effects and treatment of cognitive deficits" should be available in survivors' clinic.

Authors' Contributions

S.S.: Conceptualized the study, main lead for MCTT development, supervised the whole research process and data analysis, written the original manuscript, and edited it. R. S.: Contributed in research formulation, development of MCTT, supervising in data collection, data analysis, and editing the final manuscript. M.C.: Contributed is in data collection, data analysis, and writing the initial draft of the manuscript. S.B.: Contributed in data collection, supervision during data collection, and in technical/clinical aspects related to data. R.S.: Contributed in data collection, supervision during data collection, and in technical/

clinical aspects related to data. R.S.: Contributed as an advisor for the study, provided supervision during study, data collection, and training process. V.K.: Contributed in data collection, data analysis, and managing barriers during data collection. R.M.: Contributed in data collection, data analysis, and managing barriers during data collection. U.D.: Contributed in data collection, data analysis, and managing barriers during data collection. S.A.: Contributed in data collection, supervision during data collection, and in technical/clinical aspects related to data. V.J.: Contributed in data collection, supervision during data collection, and in technical/clinical aspects related to data. The manuscript has been read and approved by all the authors, that the requirements for authorship have been met and that each author believes that the manuscript represents honest work and that information is not provided in another form.

Patient Consent

Patient consent has been received.

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Conflict of Interest

None declared.

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