



Title: Efficacy of Musical Training on Psychological Outcomes and Quality of Life in Chinese Pediatric Brain Tumor Survivors

Ankie T. Cheung MPhil RN
School of Nursing
The University of Hong Kong

William H.C. Li PhD RN
School of Nursing
The University of Hong Kong

Ka Yan Ho, PhD RN
School of Nursing
The University of Hong Kong

Katherine K.K. Lam PhD RN
School of Nursing
The University of Hong Kong

Laurie L. K. Ho, MPhil RN
School of Nursing
The University of Hong Kong

S.Y. Chiu, MPH RN
Paediatric Oncology Unit,
Queen Mary Hospital, Hong Kong

Godfrey C.F. Chan, MRCP, FHKAM, FHKCPaed
Department of Adolescent Medicine
Queen Mary Hospital

O. K.Chung, PhD, RN
School of Nursing
The University of Hong Kong

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Corresponding author:
Dr. Ho Cheung William LI
Associate Professor
School of Nursing
The University of Hong Kong
4/F, William M. W. Mong Block,
21 Sassoon Road, Pokfulam, Hong Kong.
Tel No. (852) 91761546
Email: william3@hku.hk

Abstract

Background: Evidence has shown that survivors of pediatric brain tumors have more negative psychological sequelae, particularly depression, than do survivors of other childhood cancers.

This study examined the efficacy of a musical training program in reducing depressive symptoms, and enhancing self-esteem and quality of life in Hong Kong Chinese pediatric brain tumor survivors.

Methods: A prospective randomized controlled trial, two-group pretest and repeated post-test, between-subjects design was conducted to 60 pediatric brain tumor survivors (8- to 15-year-olds). Participants in the experimental group received a weekly 45-minute lesson on musical training for 52 weeks. Participants in the control group received a placebo intervention. The primary outcome was depressive symptoms at 12 months. Secondary outcomes were self-esteem and quality of life at 12 months. Data were collected at baseline, and 6 and 12 months after the intervention began.

Results: Participants in the experimental group reported statistically significant fewer depressive symptoms ($P < .001$), higher levels of self-esteem ($P < .001$), and better quality of life ($P < .001$) than the control group at 12-month follow-up.

Conclusions: This study provides evidence that musical training is effective in reducing depressive symptoms, and enhancing self-esteem and quality of life in Hong Kong Chinese pediatric brain tumor survivors. These results indicate that musical training is not only a leisure activity, but carries therapeutic effects in promoting psychological well-being and quality of life in pediatric brain tumor survivors.

Keywords: Brain tumors; Cancer; Childhood cancer survivors; Depressive symptoms; Oncology; Quality of life; Self-esteem

Introduction

With the advances in cancer screening and medical treatment, the survival rates for all types of childhood cancer are now higher than ever before [1]. Nevertheless, a large body of evidence shows that cancer and its treatments have long-term and lasting adverse effects on the psychological well-being and neurocognitive functioning of childhood cancer survivors [2,3]. In particular, survivors of pediatric brain tumors reportedly have more negative psychological and cognitive sequelae than do survivors of other childhood cancers [4]. The long-term neuropsychiatric conditions in cancer survivors, such as depression, anxiety, and behavioral and social problems, may result from damage to neural cells as a result of a brain tumor or its treatment, as well as potential interactions with psychological adjustments [4,5]. Of these adverse psychiatric conditions, depression is the most commonly experienced symptom by survivors of pediatric brain tumors [4]. A systematic review of 17 research papers with 5320 survivors of pediatric brain tumors revealed these individuals to have significantly higher depressive scores than survivors of any other cancer type [4]. Additionally, survivors of pediatric brain tumors are more than 2.6 times, as likely to develop depression, than their sibling counterparts [6]. Evidence indicates that high level of depression experienced by pediatric brain tumor survivors could be attributed to the combined effect of cancer diagnosis with comparatively poor prognosis, worry for recurrence, and impaired physical, neurocognitive, and psychosocial functioning [7].

As well as depression, potential late effects in childhood brain tumor survivors, such as distorted self-esteem, remain a profound concern. Self-esteem has been regarded as a vital element of one's psychosocial well-being [8]. A cohort study with 697 adult survivors of pediatric brain tumors found that the survivors possess significantly lower levels of self-esteem than healthy individuals [9]. This may be a result of persistent changes in survivors' physical appearance, including presence of visible scars, hair loss or even long-term alopecia, head or neck disfigurement, and short stature [10].

Pediatric brain tumors survivors' quality of life is severely compromised due to the devastating effects imposed by the tumor and sequelae of its treatment which appear across domains of cognitive, physical, and psychological functioning [4,5]. Coping with psychological sequelae is a distressing experience for survivors of pediatric brain tumors, leading to long-term decrement of their quality of life [11].

Although pediatric brain tumor survivors in Hong Kong receive regular medical follow-ups after completing the entire course of cancer treatment, these principally focus on their physiological health. At present, there is a lack of intervention studies that aim to promote psychological well-being, such as reducing depressive symptoms and enhancing quality of life. A review of the literature has revealed that, no study to date has investigated how non-pharmacological interventions might alleviate the psychological sequelae in pediatric brain tumor survivors in Hong Kong.

There has been an increase in the use of musical training to promote neuro-rehabilitation of patients with stroke and Parkinson's disease [12,13], and to alleviate depressive symptoms in hospitalized children [14]. Moreover, musical training has been found to enhance children's self-esteem [15]. Self-esteem is defined as an individual's self-evaluation and perception of his or her value, ability, and self-worth in relation to the appraisal and feedback received from others and from society [8]. Unlike other play activities, musical training is an activity that calls upon a wide variety of skills, such as attention and motor control of musical instruments, memorizing long musical passages, and translating the passages into sequential, bimanual motor activities. The development and acquisition of musical skills from musical training is thus a significant personal accomplishment [16,17]. According to McCormick and McPherson [18], this sense of achievement is particularly crucial in the development of positive self-esteem.

Musical training has also been found to be effective in reducing depressive symptoms in patients with psychiatric illness [14]. Musical training allows children to process their negative emotions in an alternative, non-verbal way when they cannot find words to express themselves [14]. Furthermore, musical training is enjoyable because of the involvement of the limbic system [19]. Specifically, it stimulates the secretion of dopamine, a neurotransmitter that creates pleasurable sensations [20], thus provoking positive mood change [21] and a relaxation response [22]. Therefore, musical training has been considered

an effective method for minimizing symptoms in a number of diseases that involve dopaminergic dysfunction, including depression [23].

There is some evidence that childhood depression may be caused by negative psychological traits, such as low self-esteem [24]. In addition, a previous study showed that higher self-esteem in childhood cancer survivors was associated with lower depressive symptoms and better quality of life [25]. Nevertheless, it is unclear whether musical training can be used to enhance self-esteem, reduce depressive symptoms, and improve quality of life in pediatric brain tumor survivors. There is an imperative need for rigorous empirical scrutiny of the efficacy of musical training. This study aimed to examine the efficacy of musical training on depressive symptoms, level of self-esteem and quality of life in Hong Kong Chinese pediatric brain tumor survivors.

Methods

Design

We conducted an RCT using a two-group pre-test and repeated post-test between-subject design. Participants were recruited from the largest pediatric oncology outpatient clinic of an acute public hospital in Hong Kong. The study period, including recruitment and data collection was from 1 February 2017 to 30 June 2018.

Participants

Hong Kong Chinese pediatric brain tumor survivors who had a baseline Center for Epidemiological Studies Depression Scale for Children score of 16 or above, and a Modified Mini-Mental Scale (MMSE) score of 18 or above (to ensure that participants had the capability to receive musical training) were invited to participate in the study. The modified MMSE is a widely used tool to assess individual's mental status. The possible range of scores is from 0 to 37, with a cut-off score of 17 or lower indicating moderate to severe cognitive impairment of children [26]. Others inclusion criteria were as follows: (1) survivors who have completed cancer treatment at least 2 months previously; (2) aged between 7 and 16 years; (3) able to speak Cantonese and read Chinese; and (4) those who did not undertake any musical training before. We excluded survivors with evidence of cancer recurrence or second malignancy in their medical records. Participants were assessed for expiratory function and fine motor skills to ensure that the experimental group would be receptive to musical training. These assessments were performed by one of the research team members and the executive director of the Music Children Foundation, and a musician with more than 25 years musical teaching experience.

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According to the Hospital Authority [27], an average of only 25 children developed brain tumors from 2011 to 2014 in Hong Kong. Due to the rarity of brain tumors in children and adolescents in Hong Kong, the sample size was based on the availability and voluntary participation of eligible participants. A total of 60 pediatric brain tumor survivors were eventually recruited.

Randomization and Masking

Participants were randomly allocated to the control or experimental group. Randomization was performed by a research team member who opened a serially labelled, opaque, sealed envelope, which contained a card indicating the randomly allocated group. That team member was independent of those who recruited participants and provided interventions. The random numbers used for group assignment were generated before participant recruitment by another research team member using a personal computer. Allocation concealment was ensured. To ensure privacy and prevent the possibility of interactions between the two groups, participants received detailed information by phone about the intervention in which they would be participating. This was an open-label trial because participants were not blinded to the group assignment.

Interventions

Experimental Group

Participants in the experimental group received a weekly 45-minute lesson on musical training for 52 weeks. Training was conducted by the Music Children Foundation, which is a non-governmental organization established by a group of professional musicians with the objectives of transforming children's lives and instilling positive values in the entire community through music. The Foundation currently provides free training on musical instruments to low-income children and children with chronic diseases.

One-to-one musical training was conducted by qualified orchestral performers at the participants' homes. The participants were assigned a particular musical instrument to learn, and this was based on their interests as well as their capability (e.g. fine motor skills and expiratory function), which was assessed by the training musician. The musical training was implemented at the participants' homes to facilitate favorable learning environments.

Training began at the lowest level (hitting simple notes) and ended at the highest level (able to play an entire song). The participants continued to the next level if they passed the relevant test; those who did not were encouraged to repeat tests.

To ensure that the intervention has an adequate effect on outcomes, an advisory committee was set up to develop the musical training intervention protocol. Please see online supplemental materials for the intervention protocol and the methods to safeguard the fidelity of musical training.

Placebo Control Group

Participants in the control group were invited to participate in a placebo control intervention.

This intervention was designed to mimic the same amount of time and attention required by the experimental group, but to have no specific or a minimal effect on the dependent variables of the study. As in the experimental group, participants received a weekly 45-minute home visit for 52 weeks by the research assistants. During the home visit, participants were engaged in several unstructured leisure activities such as playing card games or chess, or watching online videos, drama series, or movies.

After the baseline assessment, participants in both the experimental and control groups received an information pamphlet about mental health (Chinese version), published by the Central Health Education Unit of the Hong Kong Department of Health. Professional counselling hotline numbers were provided in the information pamphlet.

Measures

Center for Epidemiological Studies Depression Scale for Children (CES-DC)

The primary outcome was depressive symptoms at 12 months, which was measured by using the Chinese version of the CES-DC [28]. It consists of 20 items that are rated on a 4-point Likert scale regarding the participants' feelings and experiences of the past week. The range of possible scores is 0 to 60, with higher scores indicating a higher risk of depression. A score of 16 or greater is indicative of a significant level of depression [29,30].

The Chinese version of the Rosenberg self-esteem scale (RSES)

Secondary outcomes were self-esteem and quality of life at 12 months. The RSES is a tool designed to measure the global self-esteem of children [31] and adolescents [32]. The scale contains 10 items, which are rated on a 4-point Likert scale, with total possible scores ranging from 10 to 40. Higher scores indicate higher levels of self-esteem.

Pediatric Quality of Life Inventory 4.0 Generic Core Scale (PedsQL 4.0)

Participants' quality of life using the Chinese version of the PedsQL 4.0, which consists of 23 items. Participants indicated how frequently they had experienced a stated problem over the last month using a 5-point Likert scale from 0 (never) to 4 (almost always). A score may range from 0 to 100, with higher scores indicating better health-related quality of life [33].

Ethical Issues

This study was approved by the Institutional Review Board of the University of Hong Kong and Hospital Authority of Hong Kong West Cluster (reference, UW 16-023).

For details of recruitment and data collection procedures, please see online supplemental materials.

Statistical analysis

All statistical analyses were conducted using SPSS version 23.0 for Windows (IBM Corp., Armonk NY, USA). We adopted the intention-to-treat approach in the analysis. Descriptive statistics were used to calculate the mean scores, standard deviations, and score ranges of the

various scales. The comparability of the two groups was assessed using inferential statistics, including independent t-tests and chi-squared tests. A mixed between-within-subjects analysis of variance (ANOVA) was conducted to examine the effect of the interventions on the study outcomes. Post-hoc pairwise comparisons using the Tukey test were conducted to compare group mean scores if significant effects were observed.

Results

A total of 78 pediatric brain tumor survivors who attended the pediatric oncology outpatient clinic and their parents expressed interest in joining the study. Of these, 15 participants had a CES-DC score less than 16, and 3 had an MMSE score less than 18, and were therefore excluded from the study. The remaining 60 survivors (8–15-year olds) were randomly assigned to the experimental (30) or control (30) groups.

One participant in the experimental group discontinued the trial due to cancer recurrence and three participants in the placebo control group dropped out due to lost interest in the study. Thus, the attrition rate was 6.7%. Those who dropped out and those who completed the study did not differ with respect to demographic data, clinical characteristics, or baseline data.

The attendance rates for both groups were high. In the experimental group, 24 participants (80%) attended all training sessions; 3 (10%) were absent from one session, 2 (6.7%) from two sessions, and 1 (3.3%) from three sessions. In the control group, 25

participants (83.3%) joined all sessions; 3 (10%) were absent from one session, and 2 (6.7%) from two sessions.

There were no significant differences in the demographic, clinical, or baseline data between the experimental and control groups (Table 1). Table 2 summarizes the findings of primary and secondary outcomes from the mixed between-within-subjects ANOVA test.

There were statistically significant main effects for the intervention on all outcomes, indicating that the intervention group had significantly lower mean scores of depressive symptoms, and higher mean scores of self-esteem and quality of life than the control group during the 12-month study period. Following the commonly used Cohen's [34] guideline, the effect sizes for the musical training intervention on the depressive symptoms, level of self-esteem, and quality of life were moderate.

Table 3 shows the results of post hoc comparisons for depressive symptoms, level of self-esteem, and quality of life at each time point. Significant between-group differences in depressive symptoms and self-esteem were observed at T2 and T3, and statistically significant between-group differences in quality of life L was only observed at T3.

Discussion

To the best of our knowledge, this is the first study to evaluate the efficacy of musical training to reduce depressive symptoms, and to enhance self-esteem and quality of life in pediatric brain tumor survivors.

It is well documented that survivors of pediatric brain tumors suffer more negative psychological and cognitive sequelae than do survivors of other childhood cancers, and have more depressive symptoms [4]. Of the initial 78 pediatric brain tumor survivors initially recruited, 63 had a CES-DC score of 16 or above, which indicated that they experienced some depressive symptoms. A previous study on Hong Kong Chinese childhood cancer survivors revealed that 52.6% participants presented some depressive symptoms, as measured by the CES-DC, which is higher than other studies reported in the West [25]. The lack of psychosocial support for pediatric brain tumor survivors in Hong Kong might contribute to the high occurrence of depressive symptoms. Unlike Hong Kong, Western countries have abundant resources and supporting strategies to promote psychological well-being in pediatric brain tumor survivors and their family members. These include social network support groups [35], and physical and psychosocial support programs, such as rehabilitation therapy, music therapy, and yoga, special educational programs led by qualified teachers [36].

A large body of evidence has shown that engaging in moderate to vigorous intensity physical activity can help ameliorate adverse cancer treatment-related effects and promote psychological well-being and quality of life in childhood cancer survivors [37]. However, unlike survivors of leukemia or lymphoma, brain tumor survivors might suffer from physical impairments that limited their ability to perform intense physical activity. Therefore, receiving musical training may be an alternative, but more feasible activity to promote their

psychological well-being and quality of life.

The mean level of depressive symptoms for participants in the experimental group was decreased from 20.60 (baseline) to 15.03 (at the 12-month follow-up), which is lower than the cut-off score of 16. This highlights the clinical significance of musical training in reducing depressive symptoms. It is likely that the effects of the musical training may be sustained over an extended period. In particular, survivors' perception of the benefits of engaging in regular musical training may reinforce the adoption and maintenance of regular participation in musical training.

Unlike depressive symptoms and self-esteem, the quality of life of pediatric brain tumor survivors in the experimental group was significantly better than the control group at the 12-month follow-up. This is in accordance with previous studies [37,38], whereby improvements in quality of life may require longer to emerge.

The findings are in accord with previous studies [14,15], which contributes to the evidence that musical training can help reduced depressive symptoms, enhance self-esteem, and promote quality of life. Most importantly, this study generates new evidence on the efficacy of musical training in promoting psychological well-being and quality of life in pediatric brain tumor survivors.

Limitations

This study had some limitations. First, all participants were recruited from one pediatric oncology unit. Although this is one of the two largest pediatric oncology units for childhood cancer survivors in Hong Kong, the sample selection might limit the generalizability of the results. Additionally, this study did not incorporate power analysis to calculate the sample size. With a sample of 60, the study might have been underpowered, and the findings can only be regarded as 'preliminary'. Although the population size for pediatric brain tumors in Hong Kong is small, future studies should aim to study larger samples, particularly to examine the relationship between musical intervention and survivors' quality of life.

Implications for practice

This study provide evidence that highlights the potential for music-based rehabilitation treatments to alleviate the psychological sequelae for these pediatric brain tumor survivors.

The results of this study may help inform parents and healthcare professionals that musical training is not only a leisure activity, but carries therapeutic effects. Moreover, the findings promote accountability and responsibility among healthcare professionals caring for pediatric brain tumor survivors through evidence-based practice. Healthcare professionals may need to look beyond their usual roles and form multidisciplinary partnerships with non-profit voluntary organizations to sustain long-term musical training programs. The government could also provide more resources and supporting strategies to promote psychological well-

being among pediatric brain tumor survivors and their family members.

Conclusion

This study delineates the feasibility, acceptability, and efficacy of musical training interventions in reducing depressive symptoms, and enhancing self-esteem and quality of life in pediatric brain tumor survivors.

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Table 1. Demographic and clinical characteristics by groups (N = 60)

	<i>n</i> (%)		χ^2	<i>p</i> -value
	Experimental group (<i>n</i> = 30)	Control group (<i>n</i> = 30)		
Sex			0.000	1.000
Male	17 (56.7)	18 (60.0)		
Female	13 (43.3)	12 (40.0)		
Treatment received			0.381	.827
Surgery	10 (33.3)	11 (36.7)		
Radiotherapy	2 (6.7)	1 (3.3)		
Chemotherapy	0 (0.0)	0 (0.0)		
Mixed method	18 (60.0)	18 (60.0)		
Time since treatment was completed			0.879	.972
6-12 months	11 (36.7)	10 (33.3)		
13-24 months	5 (16.7)	4 (13.3)		
25-36 months	3 (10.0)	5 (16.7)		
37-48 months	3 (10.0)	4 (13.3)		
49-60 months	1 (3.3)	1 (3.3)		
>60 months	7 (23.3)	6 (20.0)		
Parents' educational attainment			0.912	.823
Primary school or below	3 (10.0)	3 (10.0)		
Lower secondary school	6 (20.0)	7 (23.3)		
Upper secondary school	13 (43.3)	15 (50.0)		
Tertiary education	8 (26.7)	5 (16.7)		
	<i>Mean (SD)</i>		<i>t</i> value	<i>p</i> value
Age of children (years)	12.53 (3.18)	13.97 (3.26)	-0.521	.605
Depressive symptoms	20.60 (7.44)	20.43 (7.23)	0.088	.930
Self-esteem	24.33 (5.86)	24.70 (6.14)	-0.237	.814
Quality of life	66.59 (12.92)	66.52 (13.13)	0.022	.983

Table 2 The results of mixed between-within subjects analysis of variance on depressive symptoms, self-esteem and quality of life scores in PBTS across the three periods (n = 60)

	Time effect				Interaction effect (time and intervention)							
	F- valu	p- valu	Eta Squa red	Po wer	F- valu	p- valu	Eta Squar ed	Pow er	F- valu	p- valu	Eta Squar ed	Pow er
Depressive symptoms	12.879	.000	.311	0.996	26.854	.000	.485	1.00	4.659	.035	.074	.565
Self-esteem	11.129	.000	.281	.989	14.298	.000	.334	.989	6.162	.016	.096	.685
Quality of life	28.745	.000	.502	1.00	49.663	.000	.635	1.00	4.036	.049	.065	.506

Table3 The results of post-hoc comparisons using the Tukey procedure for depressive

symptoms, self-esteem and quality of life scores across the three periods (n = 60)

	Depressive symptoms		p- valu	Self-esteem		p- valu	Quality of life		p- valu
	Interventiona 1 (n=30) M (SD)	Contro l (n=30) M (SD)		Interventiona 1 (n=30) M (SD)	Contro l (n=30) M (SD)		Interventiona 1 (n=30) M (SD)	Control (n=30) M (SD)	
T 1	20.60 (7.44)	20.43 (7.23)	.930	24.33 (5.86)	24.70 (6.14)	.814	66.59 (12.92)	66.52 (13.13)	.983
T 2	16.27 (6.24)	21.10 (7.55)	.009	28.87 (4.56)	24.37 (5.14)	.001	71.96 (12.06)	65.07 (14.89)	.054
T 3	15.03 (5.39)	21.47 (7.16)	.000	29.63 (4.33)	24.37 (5.24)	.000	78.12 (11.76)	64.93 (14.11)	.000

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