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Associations between leisure-time physical activity and health-related quality of life among adolescent and adult survivors of childhood cancers

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Abstract

Objective—Survivors of childhood cancer are at an increased risk for reduced quality of life (QOL), yet few studies have explored factors associated with improving health-related QOL (HRQOL) in this population. We thus explored the relationship between physical activity (PA) and HRQOL among survivors of childhood cancer.

Methods—A total of 215 survivors of childhood lymphoma, leukemia, and central nervous system (CNS) cancers completed mailed surveys that elicited information regarding leisure-time PA (LTPA) measured in metabolic equivalents, HRQOL, and diagnostic and demographic factors. Correlations and adjusted regression models were use to explore the relationship between LTPA and HRQOL.

Results—In the total sample, modest yet significant linear associations were observed between LTPA and overall HRQOL ($\beta = 0.17$, $p < 0.01$) as well as each of the respective subscales ($\beta = 0.11–0.23$ and $p < 0.05$ to < 0.001). Among adolescent survivors of childhood cancer, LTPA was significantly associated with overall HRQOL ($\beta = 0.27$), cancer worry ($\beta = 0.36$), cognitive function ($\beta = 0.32$), body appearance ($\beta = 0.29$), and social function ($\beta = 0.27$) (all $p < 0.05$). Among adult survivors of childhood cancer, LTPA was only significantly associated with physical function ($\beta = 0.28$, $p < 0.001$).

Conclusions—Significant associations exist between LTPA and HRQOL; however, the association was stronger and observed in more domains for adolescent survivors of childhood cancer. More research is needed to determine the antecedents and consequences of physical activity in this population.

Keywords

childhood; neoplasms; physical activity; quality of life; survivor

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INTRODUCTION

Health-related quality of life (HRQOL), an important end point in cancer clinical trials, is a multidimensional construct composed of physical, mental, and social dimensions [1,2]. As more studies are published regarding the late effects experienced by cancer survivors, especially survivors of childhood cancers, it is becoming increasingly apparent that this population of cancer survivors report significantly lower levels of physical, mental, social, and emotional functioning than age- and gender-matched peers [3–9]. For example, Schultz et al. [10] observed that compared with healthy siblings, survivors of childhood cancer are 1.7 times more likely to report antisocial behavior and 1.5 times more likely to report anxiety or depression. In addition, survivors of childhood cancer are three times more likely than siblings to report limitations in physical function and 20 times more likely to report disabilities [8,9]. Furthermore, neurocognitive deficits are reported in roughly half of all children treated for cancer [3,11,12].

Encouragingly, increasing physical activity (PA) may help mitigate some of the treatment-related sequelae experienced by survivors of childhood cancer and improve HRQOL [13]. While, the protective effects of PA are confirmed in adult cancer survivors [14–21], few have examined the HRQOL benefits associated with PA among survivors of childhood cancers. In one cross-sectional study of adolescent survivors (n = 53) of childhood leukemia, lymphoma, and central nervous system (CNS) cancers, Keats et al. [22] observed that those who were physically active before, during, and after treatment had higher self-concept and physical function scores than did survivors with more sedentary activity patterns before, during, and after treatment. In addition, two recent prospective studies of survivors of pediatric and adolescent cancers reported that participation in a PA intervention was associated with improvement in fitness, muscular strength, fatigue, and mental and physical health [23,24].

The preliminary evidence linking PA to HRQOL among survivors of childhood cancers is promising; however, in previous studies, very small sample sizes (range, 7–53) were used to explore relationships, and several studies were conducted among only a subset of survivors (e.g., survivors of acute lymphoblastic leukemia). Therefore, we sought to explore such associations in a larger, more diverse sample of survivors of childhood cancer—those diagnosed with leukemia, lymphoma, and CNS tumors and survivors who were currently of adolescent and adult ages. Establishing a relationship between PA and HRQOL among survivors of childhood cancer is a preliminary step to the creation of PA interventions designed to improve HRQOL and to reduce adverse treatment effects.

MATERIALS AND METHODS

Study population

Potential survivors were identified from the Central Cancer Registry, the Brain Tumor Center, the Young Cancer Survivors Program, and the Children’s Cancer Center at Duke University Medical Center, Durham, NC. We identified survivors of childhood cancer who met the following criteria: (a) previously diagnosed with lymphoma, leukemia, or a CNS cancer; (b) between 11 and 33 years old at the time of survey; and (c) with no evidence of recurrent or progressive disease at least 1-year post treatment. Permission was secured from oncology care physicians before potential participants were contacted. All participants were contacted by way of mail, with adult survivors addressed directly, and legal guardians serving as points of contact for survivors under the age of 18. Each mailed packet contained a cover letter, consent form (assent for minor-aged survivors), 11-page survey, preaddressed postage-paid return envelope, and cash incentive of $10. Guardians were asked to pass-on child-addressed packets to their children for completion.

A total of 497 surveys was sent between July and November 2003, and completed surveys were received until February 2004. We later learned that 90 subjects were unable to be contacted at the addresses provided by the tumor registry, 17 subjects were not eligible because of diagnosis or age, and 10 subjects were deceased. Therefore, our total potential sample pool included 380 survivors. The study protocol was reviewed and approved by the Human Subject Committee of Duke University Medical Center and the North Carolina Central Tumor Registry.

Study variables

HRQOL was measured using the Pediatric Quality of Life (Peds QL) Generic Core (physical function [8-items], social function [5-items]), and Cancer Module (cognitive function [5-items], pain and hurt [2-items], worry [3-items], and body appearance [3-items]) Subscales [25–28]. Modifications were made to ensure that items were conceptually similar for all age groups in our sample to facilitate subscale comparisons across age groups and to ensure developmentally appropriate language. For example, one item on the cognitive function subscale was changed by omitting the word “school” from the following item:“I have trouble writing (school) papers or reports.” Several adaptations were made to items on the social function subscale and these are reported in Appendix A. Similar modification for a young adult population was reported elsewhere [25,27,28]. Each subscale was ranked on a 5-point Likert response scale from 0 (never a problem) to 4 (always a problem). Summative scores were computed by reverse scoring and transforming each item to a scale of 0 to 100 (0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0), with higher scores indicating better HRQOL. The general PedsQL and its cancer module have demonstrated reliability and validity among survivors of childhood cancer [1]. The feasibility, reliability, and validity of a modified version of the PedsQL generic core scales, cancer module, and the PedsQL Multidimensional Fatigue scale was confirmed in a healthy young adult population and populations of young adults with chronic conditions [25,27,28], suggesting that our modifications are appropriate for a population of young adult survivors of childhood cancers. Internal consistency coefficients for the subscales in our study were in the range of $\alpha = 0.73–0.89$ for adolescents and $\alpha = 0.66–0.88$ for adults. Small to moderate correlations were observed among our subscales indicating discriminate validity.

Leisure Time Physical Activity (LTPA)—The Godin Leisure-Time Exercise Questionnaire (GLTEQ), an instrument with proven reliability and validity, was used to measure PA [29,30]. The GLTEQ elicits information regarding the frequency of strenuous, moderate, and mild PA for more than 15 minutes per day during leisure time. Given that our adolescent and young adult participants largely resided in the southeastern United States, a few of the example items were modified to better fit the population of study (e.g., horseshoes and snowmobiling were totally eliminated and the following metabolic equivalent substitutions were made: jump rope for squash, martial arts for judo, roller-blading for cross-country skiing, gymnastics for folk dancing, and skateboarding for badminton). To create MET values, the frequencies were weighted, each frequency by intensity, and values were summed for a total score (i.e., 3 × mild + 5 × moderate + 9 × strenuous).

Study covariates—Covariates included age, gender, race, cancer type, years from diagnosis, and body mass index (BMI) risk category. With the exception of height and weight, demographic and diagnostic variables were obtained from the tumor registry before the survey was administered. Heights and weights were self-reported by participants. For participants who were 20 years old or younger, Centers for Disease Control and Prevention age- and gender-specific cut points were used to categorize survivors by BMI strata [31]. Adolescents with BMIs below the 5th percentile were classified as underweight, those with

BMIs between the 5th and 84th percentiles were classified as normal, those with BMIs between the 85th and 94th percentiles were classified as overweight, and those with BMIs at the 95th percentile or higher were classified as obese. Adult BMI descriptions (e.g., obese) were applied for consistency purposes. Standard BMI (kg/m^2) cut points (e.g., overweight and obese) were applied for participants 21 years of age and older.

Data analysis

Means and standard errors were initially computed for all demographic characteristics. Proportional and mean differences in patient characteristics between age groups were explored using χ^2 and non-parametric test, respectively. We examined the normality of the HRQOL and LTPA scales prior to performing t-test to determine if there were age group (< 18 years old versus 18+) differences between means. Pearson correlations were then computed to assess the relationship between LTPA and the HRQOL indicators within the total sample and then separately for adolescents and adults. Adjusted general linear models were then computed to explore associations between LTPA and HRQOL indicators within the total sample and then separately for adolescents and adults. Covariates included in the general liner models were age (continuous), gender, time since diagnosis, BMI risk, and cancer type. Given the sample size, only main effects were assessed. All data were analyzed using SAS version 9.13 software (SAS, Cary, NC), and statistical significance ($p < 0.05$) was determined using two-sided test.

RESULTS

Sample characteristics

Among a sample of 380 eligible adult and adolescent-aged survivors of childhood leukemia, lymphoma and CNS cancers, complete data were obtained for 215 survivors (57% response rate). No significant differences were observed between respondents and nonrespondents on the basis of age, gender, race, disease category, or time elapsed since diagnosis. Characteristics of the study sample, reported in Table 1, suggest that racially the sample was mostly white, but cancer type, race, and gender were equally distributed between the adolescents and adults and among cancer types. Few differences existed between adult and adolescent survivors and among cancer types. Adults were further from time of diagnosis, diagnosed at a later age, and body mass index was generally higher than adolescents were. Among cancer types, Lymphoma survivors were generally older and diagnosed at a later age.

LTPA and HRQOL subscales by age group

No significant differences were observed between adult and adolescent survivors of childhood cancer for overall HRQOL, physical function, social function, pain, cognitive function or body appearance; however, adolescent survivors performed better in terms of cancer worry and LTPA ($p < .05$).

Associations between LTPA and HRQOL

Coefficients (Pearson's *r* and standardized β) that describe the associations between LTPA and overall HRQOL and individual subscales are presented in Table 3. In the total sample, LTPA was significantly associated with overall improved HRQOL and with each of the HRQOL subscales. Regression models generally yielded more conservative estimates than did Pearson testing (adjusted βs ranged from .11 to .23, compared with *r*s, which ranged from .16 to .35); however, all findings were statistically significant (all $p \leq 0.02$).

Furthermore, in subgroup analyses conducted separately for adolescents and adults, strong correlations continued to be observed between LTPA and improved overall HRQOL;

however, several differences in the regression models were noted between the groups for the various HRQOL subscales. For example, LTPA was associated only with improved physical function among adult survivors of childhood cancer ($p < 0.01$), whereas LTPA was significantly associated with improved overall HRQOL, social function, cognitive function, cancer worry, and body appearance in adolescent survivors of childhood cancer (all $p < 0.01$).

DISCUSSION

This cross-sectional study examined the relationship between LTPA and HRQOL in a sample of adult and adolescent survivors of childhood cancers. The results of our study indicated that adult and adolescent survivors did not differ terms of overall HRQOL, physical function, social function, cognitive function, and body appearance; however, adolescents reported better cancer worry scores and more LTPA than adults [32]. The HRQOL data obtained from our sample are similar to the normative data published by Varni et al. [26]. The overall mean HRQOL score reported by Varni et al. [26] was 72.2 ± 16.4 compared to our overall mean score of 72.0 ± 17.2 and suggest that our population scores are a full 10-points lower than age-matched healthy populations. In addition, we found that LTPA was positively associated not only with better overall HRQOL but also with each of the six individual subscales. In separate analyses for adult survivors, LTPA was significantly associated only with physical function, whereas for adolescent survivors, significant positive associations were found in far more domains (i.e., overall HRQOL, social function, cognitive function, cancer worry, and body appearance). There was a borderline association for physical function. Overall, our results suggest that there are age-specific relationships between LTPA and HRQOL in survivors of childhood cancers.

Recent studies among adolescent survivors of childhood cancer suggest that PA is associated with several health benefits [22–24,33–38]. Prospective studies in this population suggest that PA is associated with improvements in cardiovascular fitness [23,24,37], muscular strength [23,24,36], flexibility [36], range of motion [36], fatigue [23,33], sleep quality [23,34], physical function [23,24], emotional function [23], and psychological health [23]. The results of our study suggest a similar pattern of relationships for our HRQOL outcomes. We found the strongest relationships between LTPA and improved HRQOL for the subscales of physical function, cognitive function, and cancer worry. Therefore, participating in PA may help to improve or preserve physical function, contribute to cognitive function performance, and reduce cancer-related worry.

The physical function benefits of PA were confirmed in prospective studies [23,36]. PA may improve self-reported physical function through its influence on cardiovascular fitness, range of motion, and muscular strength [23,24,36,37]. In our study, LTPA was associated with physical function in the overall sample and among adults but not among adolescents, suggesting either that our study lacked appropriate power to discern this association (a real possibility given that a borderline association was found) or that this relationship was confounded by other variables. If the results we observed here and those of prospective studies hold true, it is logical that participating in PA may help to improve or preserve physical function outcomes among survivors of childhood cancer [3,7–9].

We believe that the relationship observed between LTPA and improved overall HRQOL among adolescents was driven primarily by the significant associations observed between LTPA and social function, cognitive function, and cancer worry. Some of these relationships are consistent with previous observations in adolescent survivors of childhood cancers [17,22,23,39]. For example, in a cross-sectional study of adolescent survivors of leukemia, lymphoma, and CNS tumors, those who were active before, during, and after cancer

treatment reported better relationships with peers [22]. In addition, Keats and Culos-Reed [23] observed in a prospective study that participation in a 16-week PA intervention was associated with an increase in social health. We can only speculate that this effect is the result of survivors of childhood cancer participating in PA in peer groups or environmental settings that provide social interaction.

The relationship observed between LTPA and cognitive or work function (i.e., cognitive function) was unexpected. In a recent prospective study among 10 adolescents with cancer [23], a 16-week intervention was not significant associated with improvement in cognitive function outcomes. Conversely, PA was associated with cognitive function in samples of health youth [40,41]. For example, a recent descriptive study among 259 third- and fifth-grade students revealed that aerobic capacity was significantly associated with total academic achievement, mathematics achievement, and reading achievement [40]. Furthermore, participating in PA may contribute to reductions in cancer worry and improved body appearance, primarily through its influence on mood and self-esteem, since there is a consistent positive association between exercise and self-esteem [42].

The nonsignificant relationships observed between LTPA and HRQOL among adults were surprising; however, we were not the first study to observe these nonsignificant relationships. For example, Marchese et al. [43] did not observe significant relationships between objective measures of PA, functional, and HRQOL outcomes in a small sample of adolescent and young adult childhood survivors of osteosarcoma. There may be several reasons why our relationships were nonsignificant. Primarily, it may be that the variability of scores for LTPA attenuated the correlation between LTPA and HRQOL. According to our data, only 22% of our adults exceeded the minimal requirements for PA (150-minutes of moderate-intensity PA or 34 to 50 LTPA units) [44], while 34% of adolescents exceed requirements. However, it may be that our adults were not active long enough to experience the health benefits of PA or that they were experiencing activity-induced consequences (e.g., chest pain, shortness of breath, heart palpitations) because they are further out from diagnosis, limiting the benefits of LTPA [45].

The primary limitation of the present study was that the data were cross-sectional in nature; therefore, no conclusions can be made about temporal sequence. For example, we do not know whether changes in physical function are a direct result of PA or vice versa. In addition, these data were self-reported by the patients, and potential limitations such as inaccurate recall and response bias are possible. In addition, our measure of LTPA precluded us from determining minutes of mild, moderate, and strenuous PA; however, LTPA can be translated into MET-minutes of PA, where 750 MET-minutes PA is roughly equivalent to 150-minutes of moderate-intensity PA per week [43]. Furthermore, the sample lacked sufficient power to explore differences in the relationship between LTPA and HRQOL across different age groups and cancer types. We also do not know whether the relationships that we observed would be similar in other populations of survivors of childhood cancer. That said, we attempted to minimize these limitations by using validated measures [25,27,28], adjusting for covariates in our models, and stratifying our analysis by age group.

In summary, this study is one of the first to explore associations between LTPA and HRQOL among a population of adolescent and adult survivors of childhood cancer of leukemia, lymphoma, and CNS cancers. Our results suggest that LTPA is significantly associated with improved HRQOL in survivors of childhood cancer previously diagnosed with leukemia, lymphoma, and CNS tumors. In addition, the relationship between LTPA and the various HRQOL subscales differs for adolescents and adults, with LTPA appearing to be important for far more domains that affect HRQOL in adolescents than adults. This is one of the novel finding of this study and more research is needed to determine if these

associations hold over time. Although, we are not aware of the mechanisms by which PA is associated with HRQOL in this population, there is a need to promote PA early during cancer management and to ensure that it continues throughout the life of the survivor. For all populations of survivors of childhood cancer, multicomponent behavioral interventions are needed that address lifestyle behaviors in an effort to improve health and prevent further declines in HRQOL. Physicians and physical therapists in follow-up clinics should consider encouraging all survivors of childhood survivors to engage in recommended amounts of physical activity as a means of fostering overall health and social competence.

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Table 1

Sample Characteristics of Survivors of Childhood Cancer Patients Participating in this Study.

Variable	Total sample (*N* = 215)	Adults (*n* = 121)	Adolescents (*n* = 94)	*P value*	CNS (*n* = 88)	Lymphoma (*n* = 47)	Leukemia (*n* = 80)	*P value*
Current age, *M* (SD)	18.0 (4.9)	22.3 (3.5)	14.3 (1.8)	<0.001[a]	19.6 (5.2)	23.0 (5.4)	19.7 (5.8)	0.005 [a]
Age at diagnosis, *M* (SD)	8.8 (4.9)	10.2 (4.8)	6.9 (4.4)	<0.001[a]	9.1 (5.1)	10.9 (4.2)	7.2 (4.6)	<0.001[a]
Years since diagnosis, *M* (SD)	9.9 (5.5)	12.1 (5.5)	7.3 (4.3)	<0.001[a]	9.5 (4.7)	10.0 (5.4)	10.7 (6.4)	0.471[a]
Gender, n (%)				0.884				0.653
Male	111 (51.1)	53 (51.2)	48 (51.1)		40 (45.5)	30 (63.8)	41 (51.2)	
Female	104 (48.9)	58 (47.9)	46 (48.9)		48 (54.5)	17 (16.2)	39 (48.8)	
Race, n (%)				0.238				0.889
White	181 (84.2)	105 (86.8)	76 (80.9)		74 (84.1)	40 (85.1)	67 (83.8)	
Nonwhite	34 (15.8)	16 (13.2)	18 (19.1)		14 (15.9)	7 (14.9)	13 (16.2)	
Cancer type, n (%)				0.078	–	–	–	–
CNS tumors	88 (40.9)	48 (39.7)	40 (42.5)		–	–	–	–
Lymphoma	47 (21.9)	40 (33.0)	40 (42.5)		–	–	–	–
Leukemia	80 (37.2)	33 (27.3)	14 (14.9)		–	–	–	–
BMI				0.037[a]				0.983[a]
M (SD)	26.0 (6.0)	26.6 (5.9)	25.1 (5.8)		25.9 (6.4)	26.1 (5.5)	26.0 (5.8)	
Underweight, n (%)	11 (5.2)	5 (4.2)	6 (6.6)		8 (9.3)	0 (0.0)	3 (3.8)	
Normal weight, n (%)	98 (46.6)	59 (50.0)	39 (42.4)		35 (40.7)	26 (57.8)	37 (46.8)	
Overweight, n (%)	25 (20.5)	25 (21.2)	23 (19.6)		19 (22.1)	7 (15.5)	17 (21.5)	
Obese, n (%)	58 (27.6)	29 (24.6)	29 (31.5)		22 (27.9)	12 (26.7)	22 (27.9)	

M = mean; SD = standard deviation; CNS = central nervous system; NS = non-significant; age- and gender-specific cut points were used to create body mass index (BMI) categories for adolescents.

[a]denotes non-parametric Kruskal-Wallis text. Please note that similar estimates were published by Demark-Wahnefried et al. in Cancer May 15, 2005, Volume 103, Number 10, page 2173.

Table 2

Descriptive statistics for health related quality of life subscales leisure and time physical activity among adult and adolescent survivors of childhood cancers.

Measure	Score Range	Total Sample Mean (SD) N = 215	Adults Mean (SD) N = 121	Adolescents Mean (SD) N = 94	*p* value of the Difference
Overall HRQOL	17.0 – 100.0	72.0 (17.1)	71.6 (16.3)	72.5 (18.2)	0.698
Physical Function	0 – 100	74.8 (19.7)	74.4 (19.6)	75.2 (20.0)	0.760
Social Function	5 – 100	80.1 (20.3)	81.1 (20.1)	78.9 (20.7)	0.435
Cognitive Function	0 – 100	66.0 (23.8)	65.5 (23.0)	66.6 (25.0)	0.755
Pain	0 – 100	71.4 (25.4)	71.7 (24.2)	71.1 (26.9)	0.875
Cancer Worry	0 – 100	69.7 (24.8)	67.1 (23.3)	73.1 (26.7)	0.030
Body Appearance	0 – 100	70.0 (24.1)	69.7 (23.3)	70.2 (25.3)	0.880
LTPA	0 – 119	37.6 (26.0)	34.4 (26.0)	41.7 (25.6)	0.043

HRQOL = Health Related Quality of Life; LTPA = Leisure Time Physical Activity; P values are based on non-parametric Kruskal-Wallis test. Please note that similar estimates were published by Demark-Wahnefried et al. in Cancer May 15, 2005, Volume 103, Number 10, page 2173. Higher scores indicate better HRQOL.

Table 3

Unadjusted and adjusted associations between physical activity and health-related quality of life among adult and adolescent survivors of childhood cancers

	Total study sample (n= 215)				Adults (n = 121)				Adolescents (n = 94)			
Measure	**r**	**r p**	**Adjusted β (SE)**	**Adjusted p**	**r**	**r p**	**Adjusted β (SE)**	**Adjusted p**	**r**	**r p**	**Adjusted β (SE)**	**Adjusted p**
Overall HRQOL	**0.28**	< 0.001	**0.17 (05)**	<0 .001	**0.28**	0.003	0.12 (.07)	0.065	**0.29**	0.007	**0.27 (.08)**	<0.001
Physical function	**0.35**	< 0.001	**0.23 (.05)**	< 0.001	**0.45**	0 .001	**0.28 (.07)**	<0.001	0.21	0.053	0.19 (.08)	0.031¥
Social function	**0.19**	0.008	**0.11 (.05)**	0.042	0.15	0.111	0.02 (.08)	0.789	**0.26**	0.020	**0.27 (.09)**	0.003
Cognitive function	**0.24**	< 0.001	**0.18 (.07)**	0.006	**0.20**	0.037	0.10 (.09)	0.258	**0.29**	0.006	**0.32 (.11)**	0.004
Pain and hurt	**0.18**	0.014	**0.17 (.07)**	0.025	**0.25**	0.008	0.17 (.08)	0.087	0.10	0.363	0.19 (.12)	0.136
Cancer worry	**0.18**	0.011	**0.20 (.07)**	0.004	0.07	0.438	0.10 (.09)	0.290	**0.27**	0.02	**0.36 (.11)**	0.001
Body appearance	**0.16**	0.023	**0.15 (.07)**	0.036	0.14	0.146	0.05 (.09)	0.591	0.20	0.071	**0.29 (.11)**	0.008

The sample sizes may vary in each analysis due to missing data. Physical activity was measured by the Godin Leisure Time Exercise Questionnaire where metabolic equivalents were calculated. *r* = Pearson correlation coefficient; *p* = p-value; β = standardized beta coefficient; SE= standard error. Models for the total sample are adjusted for age, gender, time since diagnosis, Body mass index risk, and diagnosis. Models for adults and adolescents are adjusted for gender, time since diagnosis, BMI risk and diagnosis. ¥ denotes that the overall model was non-significant, but the physical activity beta value was significant.

Appendix A

Adapted Social Functioning Subscale from the PedsQL™ Cancer Module

In the past one month, how much of a problem has each of the following been for you?

SOCIAL FUNCTIONING	Never	Almost Never	Some-times	Often	Almost Always
I have trouble getting along with other people my age	0	1	2	3	4
Other people my age do not want to be my friend	0	1	2	3	4
Other people my age tease me	0	1	2	3	4
I cannot do things that other people my age can do	0	1	2	3	4
It is hard to keep up with my peers	0	1	2	3	4