

ACTIVITIES OF DAILY LIVING AND QUALITY OF LIFE IN SURVIVORS
OF CHILDHOOD BRAIN TUMOUR

Catherine Demers, B.Sc.
School of Physical and Occupational Therapy
Faculty of Medicine, McGill University, Montréal, Quebec, Canada
April, 2014

A thesis submitted to McGill University in partial fulfillment of the
requirements of the degree of Master of Science in Rehabilitation Science

©Catherine Demers, 2014

*"Je n'étais encore qu'une enfant
J'étais toute jeune
Je n'avais que huit ans
Je vivais pleinement ma vie
Profitant de ces petits plaisirs
Comme on la vit quand on est jeune et sans souci
[...]*

*Quand un jour, sans prévenir,
Le destin s'acharna sur moi
Se faisant discret et inquiétant
Malin et rusé, en trompait plusieurs
Donnant du fil à retordre
À tous ceux voulant le déjouer*

*Identifié à temps par des experts
Pour me sauver des bras de Lucifer
Traité comme une urgence
D'une grande importance
[...]*

*Un remède des plus dévastateurs que réparateurs
Engendrant de multiples séquelles
Créant une vie que je n'ai pas choisie
[...]*

*Prenant conscience qu'alentour le monde avait évolué
Alors que j'étais restée au même stade,
Ralentie par le poids des repercussions du périple
[...]*

*Avançant dans un monde barbare
Trébuchant, me relevant
Gardant espoir dans mon coeur et ma tête
Qu'un jour, j'atteindrai le haut de la montagne
[...]*

*Il y a 13 ans, j'étais une autre personne et je n'aurais pas été la même aujourd'hui,
Si je n'avais pas surmonté tous ces obstacles
Et avec la force que j'ai acquise,
Ça me mènera sûrement plus loin et me permettra de franchir
De nouvelles frontières."*

Poem by Audrey, a cancer survivor

ACKNOWLEDGMENTS

I wish to express my sincere gratitude to everyone who has contributed to the development and completion of this thesis. I would especially like to thank and acknowledge my supervisor, Isabelle Gélinas. I was privileged to have had receive so much support from her throughout the past three years. I would also like to acknowledge the members of my supervisory committee; Dr. Anne-Sophie Carret, Marie St-Jacques and Anne Guérette for their contribution to this project. This thesis would not have been possible without their expertise, guidance and generosity.

I would also like to extend my thanks to my colleagues from the oncology rehabilitation team at Ste-Justine Hospital, especially Diane Noël and Annie Simoneau, for their very precious expertise and support through all the steps of this research. I have the privilege of working with passionate and very supportive coworkers. As a young clinician, their love of the profession and their devotion to their patients are more than inspiring. I am also grateful for the help with statistical analyses provided by Gevorg Chilingaryan.

A special and warm thank you to the participants and their family who have used their time to share their experiences in helping to provide a greater understanding of their life after cancer. I am sincerely grateful for their time and generosity.

Last by not the least, there is still my family and friends who deserve to be duly acknowledge for their incredible support and their constant

encouragement. I would particularly like to thank Jean-Philippe for his patience and for constantly supporting me throughout my endeavours. I am thankful for being surrounded by loving people who always encourage me in the pursuit of my goals.

TABLE OF CONTENTS

DEDICATION	II
ACKNOWLEDGMENTS	III
TABLE OF CONTENTS	V
LIST OF TABLES.....	VII
LIST OF FIGURES.....	VIII
ABSTRACT	IX
ABREGE.....	XI
PREFACE	XIII
 CHAPTER 1: REVIEW OF THE LITERATURE.....	 1
1.1 CHILDHOOD CANCER SURVIVORSHIP	1
1.2 BRAIN TUMOUR	3
1.3 LATE EFFECTS	4
1.3.1 <i>Medical late effetcs</i>	6
1.3.2 <i>Neurocognitive late effects</i>	7
1.3.3 <i>Psychosocial late effetcs</i>	9
1.3.4 <i>Factors for late effects</i>	9
1.4 HEALTH-RELATED QUALITY OF LIFE	10
1.5 FUNCTIONAL IMPACT OF LATE EFFETCS	13
1.6 ACTIVITIES OF DAILY LIVING.....	14
1.7 ONCOLOGY REHABILITATION	16
 CHAPTER 2: RATIONALE, OBJECTIVES, AND HYPOTHESES	 18
2.1 RATIONALE	18
2.2 OBJECTIVES	21
2.3 HYPOTHESES	22
 CHAPTER 3: FIRST MANUSCRIPT	 23
3.1 ABSTRACT	24
3.2 INTRODUCTION.....	25
3.3 METHODS.....	27
3.4 RESULTS.....	31
3.5 DISCUSSION	33
3.6 TABLES	38
3.7 REFERENCES FOR MANUSCRIPT 1	40

CHAPTER 4: INTEGRATION OF MANUSCRIPTS.....	44
CHAPTER 5: SECOND MANUSCRIPT	45
5.1 ABSTRACT.....	46
5.2 INTRODUCTION.....	46
5.3 METHODS.....	49
5.4 RESULTS.....	55
5.5 DISCUSSION	56
5.6 TABLES AND FIGURES	62
5.7 REFERENCES FOR MANUSCRIPT 2	65
CHAPTER 6: CONCLUSION AND SUMMARY	69
REFERENCES	71
APPENDICES	81
APPENDIX A: SOCIO-DEMOGRAPHIC QUESTIONNAIRE.....	81
APPENDIX B: SF-12 QUESTIONNAIRE	83
APPENDIX C: ASSESSMENT OF MOTOR AND PROCESS SKILLS GRAPHIC REPORT ...	86
APPENDIX D: CONSENT FORM.....	87

LIST OF TABLES

TABLE 3.1: CHARACTERISTICS OF STUDY PARTICIPANTS	38
TABLE 3.2: FUNCTIONAL CHARACTERISTICS OF THE STUDY PARTICIPANTS	39
TABLE 3.3: ASSOCIATION BETWEEN MOTOR AND PROCESS SKILLS AND CLINICAL CHARACTERISTICS	40
TABLE 5.1: PERSONAL AND CLINICAL CHARACTERISTICS OF STUDY PARTICIPANTS	62
TABLE 5.2: RESULTS OF AMPS EVALUATION (ADL MOTOR AND PROCESS ABILITY) IN COMPARISON WITH AGE NORMS.	63
TABLE 5.3: RESULTS OF SF-12 QUESTIONNAIRE IN COMPARISON WITH POPULATION NORMS.....	63

LIST OF FIGURES

FIGURE 1.1: FACTORS FOR LATE EFFECTS 9

FIGURE 1.2: WILSON AND CLEARY MODEL..... 13

FIGURE 5.1: ASSOCIATION BETWEEN MOTOR SKILLS, PROCESS SKILLS,
AND MENTAL COMPONENT SCALE (MCS) AND PHYSICAL COMPONENT
SCALE (PCS) OF THE SF-12..... 64

ABSTRACT

Innovations in medical technology have led to earlier diagnoses and improved treatment of cancers, increasing the survival rate to nearly 70% for children with brain tumors (BT) in North America. Nevertheless, survivors are left to struggle with a host of issues that often leave them unnecessarily disabled or, at the very least, only able to function at a level that is not optimal. The impact of late effects on function and daily living, however, are poorly quantified. Therefore, this thesis addresses the functional outcomes and health-related quality of life (HRQoL) of adolescent and young adult survivors of childhood BT. The focus is on performance in daily living activities (ADL) and HRQoL as they reflect the everyday life of survivors beyond the acute diagnosis and treatment phases. **Objectives.** The primary objective was to estimate the extent to which young adult survivors of childhood BT achieve a level of performance in ADL that is comparable to their peers 5 years after diagnosis. The secondary objectives were: 1) to assess the association between observed limitations in motor and process skills and the HRQoL of BT survivors; 2) to determine which factors for specific impairments are likely to be associated with performance limitations. **Methods.** A cross-sectional study was conducted with a convenience sample of 36 BT survivors recruited from a long-term follow-up clinic at CHU Ste-Justine in Montreal. The Assessment of Motor and Process Skills (AMPS), a standardized objective measure, was used to evaluate the quality of ADL task performance, and a generic instrument, the SF-12 questionnaire, to measure HRQoL. **Results.** The survivors had significantly lower performance in ADL ($p<0.01$). Functional level was found to be positively associated with the physical ($r^2=0.5$) and mental

($r^2=0.3$) component scales of the SF-12. The level of functioning was associated with age at diagnosis for process skills; and gender, tumour location, time since treatment and chronic health conditions for motor skills. ***Conclusions.*** Understanding the impact of cancer and its treatment on the life of childhood cancer survivors provides foundation for the creation of specialised rehabilitation programs.

ABRÉGÉ

Les avancées médicales des dernières décennies ont menées à des diagnostics précoces ainsi qu'à une amélioration des traitements du cancer, augmentant par le fait même le taux de survie à 70% pour les enfants avec tumeur cérébrale (TC). Par contre, les survivants doivent par la suite gérer de nombreux effets indésirables qui les laissent souvent en situation d'handicap ou, au mieux, seulement capables de fonctionner à un niveau sous-optimal. L'impact des effets secondaires sur le fonctionnement et la vie quotidienne est toutefois peu quantifié. Cette thèse se penche donc sur le rendement fonctionnel et la qualité de vie reliée à la santé des adolescents et jeunes adultes survivants de tumeur cérébrale. L'emphasis est mis sur la performance dans les activités de la vie quotidienne (AVQ) et la qualité de vie reliée à la santé puisqu'ils reflètent bien la vie de tous les jours après la phase aigue et de traitements actifs. **Objectifs.** L'objectif principal était d'estimer l'étendu à laquelle les jeunes survivants de tumeur cérébrale peuvent atteindre un niveau de performance dans les AVQ qui est comparable à leurs pairs, au moins 5 ans après le diagnostic. Les objectifs secondaires sont de: 1) évaluer les associations entre les limitations observées dans les habiletés motrices et procédurales avec la qualité de vie reliée à la santé; 2) de déterminer quels sont les facteurs qui sont associés au niveau de limitations observé dans la performance occupationnelle. **Méthodologie.** Une étude transversale a été réalisée avec un échantillon de commodité comprenant 36 participants recrutés par la clinique de suivi long-terme du CHU Ste-Justine, à Montréal. L'outil d'évaluation le *Assessment of Motor and Process Skills* (AMPS), une mesure objective et standardisée, a été utilisé pour évaluer la

qualité de la performance dans la réalisation des AVQ. Un questionnaire général, le SF-12, a pour sa part été utilisé pour évaluer la qualité de vie reliée à la santé. **Résultats.** Les jeunes survivants présentent un niveau de fonctionnement dans les AVQ significativement plus bas que la norme ($p < 0.01$). Le niveau de fonctionnement était positivement associé avec l'aspect de santé physique ($r^2 = 0.5$) et mental ($r^2 = 0.3$) du SF-12. Le niveau de fonctionnement dans les habiletés procédurales a été associé avec l'âge au diagnostic. Pour les habiletés motrices, les facteurs associés sont le sexe, la localisation de la tumeur, le temps depuis la fin des traitements, ainsi que les conditions de santé chronique. **Conclusion.** Une meilleure compréhension de l'impact du cancer et des traitements sur la vie quotidienne des survivants du cancer fournit un bon point de départ pour la création de programmes de réadaptation spécialisés.

PREFACE

This thesis contains no materials that have been published elsewhere or written by someone else, except where specifically referenced. The research presented constitutes original material and contributes to the advancement of knowledge in the field of cancer rehabilitation.

Author's contributions

Prior to the completion of this manuscript-based thesis, several important steps were undertaken. At first, the thesis protocol was prepared by Catherine Demers and approved by the thesis committee members; Dr. Anne-Sophie Carret, Marie St-Jacques and Anne Guérette, and by the thesis supervisor, Dr. Isabelle Gélinas. Then, the research project was conducted, and the data collected. Finally, all the collected data was carefully examined and analyzed, with the help of Gevorg Chilingaryan. All these steps have been carried out by Catherine Demers under the supervision of Isabelle Gélinas and the guidance of the supervisory committee composed of Dr. Carret and Marie St-Jacques. The manuscripts contained in this thesis are the work of Catherine Demers with editing and feedback from Dr Isabelle Gélinas, and support from Dr. Carret and Marie St-Jacques.

Organization of the thesis

The first manuscript addresses the primary objective as well as the first secondary objective of this research. The other secondary objective is addressed in the second manuscript. These manuscripts will later be submitted to scientific journals for publications.

Additional chapters have been included in this thesis in accordance with the regulations outlined by the Graduate and Postdoctoral Studies (GPS) Office of McGill University. GPS requires that each thesis contains a literature review and conclusion that is separate from the manuscripts. Therefore, duplication of material and repetitions in this thesis is unavoidable.

The thesis is organized in 6 chapters.

Chapter 1 provides an introduction and a literature review on childhood cancer, including information regarding childhood brain tumour, late effects of cancer, health related quality of life, and oncology rehabilitation.

Chapter 2 outlines the rationale, the research objectives, and hypotheses.

Chapter 3 consists of the first manuscript. This manuscript focuses on the study's main objective, which was to estimate the extent to which long-term effects of childhood brain tumour and related treatments impact on performance in activities of daily and to determine which factors are likely to be associated with performance limitation.

Chapter 4 links the first manuscript to the second.

Chapter 5 consists of the second manuscript, which provides a comparison of the performance in activities of daily living of young adults survivors of childhood Brain Tumour (BT) with norms and explores associations with health-related quality of life (HRQoL).

Chapter 6 is a summary of the findings and conclusions of the two manuscripts.

For the manuscripts, the tables, figures and references are included at the end of the text. The references for all other chapters are presented at the end of the thesis.

CHAPTER 1: REVIEW OF THE LITERATURE

1.1 Childhood cancer survivorship

Prior to 1970, most children and young adults diagnosed with cancer had little hope of being cured [1]. Since then, the cancer mortality rate has been constantly declining as a result of the successful treatment of the most common cancers, while the cancer incidence rate in children and youth has been relatively constant since 1985 [2]. Although they account for just 1% of all cancers diagnosed in Canada, on average as many as 1,310 children and youth aged 0–19 years develop cancer each year [2]. Combined survival rate for all paediatric cancers is estimated to be 82% [2] which makes the childhood cancer survivor population significant. Indeed, it is estimated that as many as 1 adult in every 450-640 adults in North America as a whole is a childhood cancer survivor [3].

When cancer was considered incurable, the term “survivor” was used to designate family members who survived the loss of a loved one to cancer [4]. As knowledge and success in understanding cancer increased, physicians began to use a 5-year time frame to define survivorship. If cancer did not recur in the 5 years following either diagnosis or treatment, patients were considered to have become “survivors”. The term is now commonly used to describe an individual from the time of diagnosis through the remaining years of his or her life [4, 5]. The National Cancer Institute (NCI) has also expanded this definition to include caregivers, friends and family members impacted by the survivorship experience. The experience of cancer survivorship has been defined by the Lance Armstrong Foundation as living “with”, “through”, and “beyond” cancer.

Living “with” cancer refers to the experience of receiving a cancer diagnosis and any treatment that may follow, living “through” cancer refers to the extended stage following treatment, and living “beyond” cancer refers to post-treatment, long-term survivorship.

Cancer in children and youth creates a disproportionate impact on health, economic and social welfare systems, as well as placing a tremendous burden on the family of the child or adolescent affected by cancer. Improving survival of childhood and youth cancers has increased the need for long-term follow up of these late effects. This ever-growing population of cancer survivors is of significant public health importance; it is in need of medical care, public health services, and support. As this cohort of children and young adults ages, it is likely that additional late effects will emerge; and as treatments change, the population of survivors will also change and we will need to adapt to their new characteristics. Thus, ongoing surveillance is needed to link childhood treatments to adult onset late effects. The Institute of Medicine has investigated the issue of cancer survivorship care and reported the many unmet needs of those who finish acute oncology treatment in a report titled *From Cancer Patient to Cancer Survivor: Lost in Transition* [6].

Furthermore, in an effort to gain knowledge about this unique population, the Childhood Cancer Survivor Study (CCSS) was created [7]. It is composed of 20,346 individuals who survived five or more years after treatment for cancer, leukemia, tumour, or similar illness diagnosed during childhood or adolescence. It also includes approximately 4,000 siblings of survivors who serve as the comparison group for the study. This collaborative, multi-institutional study has been assembled through the

efforts of 27 participating centers in the United States and Canada, was funded by the National Cancer Institute, and is coordinated through St. Jude Children's Research Hospital in Memphis, Tennessee. The childhood cancer survivor population is increasingly studied and therefore understood, according to, among other things, this cohort.

1.2 Brain tumour

Childhood cancer is not just one disease; there are many major types, and countless subtypes, each having unique features. Childhood brain tumours (BT) are the second most common paediatric malignancy and the most common solid tumour during childhood [8]. According to Statistics Canada [9], BT is one of the most common types of cancers diagnosed in 0-14 year olds and accounts for approximately 20% of cancers in children diagnosed between 2000 and 2004. BT that occurs in infants and children are very different from adult BT, both in terms of the type of cells and the responsiveness to treatment. BT can be classified into two groups: primary and secondary. Tumours that begin in brain tissue are known as primary brain tumours and a secondary BT is a tumour that results from a cancer that originates in another part of the body. Only primary brain tumours will be considered in this thesis. The tumour can be either benign or malignant. Although in most parts of the body a benign tumour is not as serious as a malignant tumour, in the brain, both benign and malignant tumours can be serious and possibly life threatening. Accounting for almost half of all childhood BT, the most common brain tumours are gliomas; and there are several types of gliomas, including astrocytoma, ependymoma, and oligodendroglioma. There are also other types of BT

that do not begin in glial tissue, including medulloblastomas that represent approximately 20% of all BT, choroid plexus carcinoma, and craniopharyngioma [10]. BTs are classified according to their histology, but tumour location and extent of spread are important factors that affect treatment and prognosis. Medical treatment is often multi-modal, incorporating combinations of surgical resection, chemotherapy, and radiation therapy, depending on the tumour's type and location. As with other tumours in both children and adults, the first treatment is usually surgery to remove as much of the tumour as possible and for some forms of brain cancer, it may be all the treatment that's required. However, treatment is usually followed by complementary chemotherapy treatments, including radiation therapy and chemotherapy. Chemotherapy is the usual treatment for children under three years of age because the young brain is especially vulnerable to radiation damage during growth and development, [11]. Radiation therapy, can be used alone or in combination with chemotherapy. Depending on the type of tumour, some patients are treated with targeted focal radiation therapy while radiation therapy can be delivered to the entire brain and spine for tumours that have spread.

Although BTs are the second leading cause of death among children with cancer [12], advancement in diagnosis techniques and multimodal treatment approaches have increased the survival rate to nearly 70% for children with BTs [13]. Consequently, such improvements have elevated the importance of considering late effects, quality of life, and functional outcomes in the years following the completion of tumour-directed treatment [14].

1.3 Late effects

For many survivors, overcoming cancer is just the first of major hurdles to be surmounted following their diagnosis [12]. Indeed, despite the advances in research and technology, patients and survivors experience a huge number of negative physical, psychosocial, and neuropsychological side effects that can start during the treatment phase or later on and often last into adulthood [15]. Recent studies revealed that 62.3% to almost 75% of survivors reported at least 1 chronic condition, and 27.5% to 40% had a severe or life-threatening condition [16, 17]. In medicine, a late effect is a condition that appears after the acute phase of an earlier condition, and that can be caused either directly by the condition or indirectly by the treatment. The wide array of potential late effects includes complications, disabilities, or adverse outcomes that are the result of the disease process, the treatment, or both. The emergence of these late effects is largely variable; some of them can be clinically silent for a long period of time and only occur decades later, and the risk often does not plateau with aging [18]. The first articles in the literature reporting late effects of treatment come from 1952, and the first conference on delayed consequences was held in 1975. More recently, the Children's Oncology Group (COG), established in 1993, has pioneered the careful follow up of these patients across North America, resulting in carefully developed guidelines of care for survivors from childhood cancers and the study of some of their problems, such as psychosocial, cognitive, and academic achievement, and developmental issues. With the results of comparative data reported on the experiences of 10,397 survivors and of 3,034 siblings from the CCSS cohort [7], the COG published in 2003 the first version of

the *Long-Term Follow-up Guidelines*. It is a major example of multidisciplinary progress for childhood cancer survivors since it provides guidelines for late effects screening and principles of surveillance in this high-risk population. The goals of these guidelines are to promote healthy lifestyles, suggest appropriate ongoing monitoring, facilitate early detection of complications, and allow for timely interventions. Recommendations are based on scientific evidence and the collective experience of experts in the area [16, 18]. These long-term deficits the survivors are experiencing affect the whole person; they include physical, sensory, cognitive, neurological, and endocrine complications [19]. There are many possible mechanisms that can produce late effects of BT, including direct effects, such as direct injury of nerves or brain tissue, or indirect effects, such as injury to blood vessels in the brain and spine, or immunological effects.

1.3.1 Medical late effects

Medical late effects are common and have been widely documented [20-24]. Most medical late effects can be linked directly to the location of the tumour within the central nervous system and the treatment modalities used (ie, surgery, cranial irradiation, and/or chemotherapy). Medical late effects generally fall into 1 of the following 5 categories: (1) physical, (2) endocrinologic, (3) neurologic, (4) sensory, and (5) secondary malignancies.

Physically, adult survivors of childhood BT have on average significant muscle weakness and poor exercise tolerance, as well as increased risk for health-related impairments associated with inactivity [25]. Furthermore,

49% of childhood cancer survivors report coordination and motor control difficulties [24, 26]. As for their physical appearance, permanent changes are common, such as visible scars from craniotomies or other surgical procedures, alopecia, and noticeable changes to the bone structure of their skull [12]. Additionally, a study reported that nearly 40% of adults who were former childhood brain tumour survivors were below the 10th percentile for adult height [22]. Many brain tumour survivors are particularly self-conscious about these physical changes, which are daily reminders of their experience [27].

Because the hypothalamic/pituitary axis is a critical center in the endocrine system, disruption of these pathways by a brain tumour or its treatment is common; the prevalence of endocrinopathies is more than 40% in paediatric patients treated for central nervous system tumours [22]. Long-term neurological impairments include strokes, seizures, peripheral neuropathy, motor dysfunction as well as posterior fossa syndrome [21, 28]. Neurosensory system late effects are also common in brain tumour survivors; effects on vision, hearing, and pain have been well documented [29-31]. Finally, a rare but often devastating medical late effect of treatment is the development of a secondary malignancy that usually occurs many years after the completion of treatment. The majority of these secondary malignancies are either gliomas, or meningiomas [32], sarcomas [33], or nonmelanoma skin cancers [34].

1.3.2 Neurocognitive late effects

The neurocognitive late effects develop and progress for years after the completion of treatment, extending into adolescence and adulthood.

Changes noted are associated with a slower-than-expected rate of development or a developmental stagnation, rather than a regression or a loss of skills. For example, medulloblastoma survivors acquire knowledge at 50% to 60% of the expected rate relative to population norms [35]. Children treated for brain tumours tend to exhibit pervasive and substantial deficits in both broad and specific neurocognitive domains, including attention, working memory, processing speed, visual-spatial skills, memory, executive functioning, and academic functioning[36, 37]. Deficiencies in the development of white matter secondary to radiation are also associated with deficits in IQ [38]. Indeed, it has been documented that deficits begin to emerge as early as 1 year post-treatment and decline of 2 to 4 IQ points per year for up to 4 years post-treatment [39]. Medium-to-large effect sizes for deficits in overall cognitive ability, verbal intelligence, and non-verbal intelligence suggest that survivors are performing almost a full standard deviation below expected based on normative levels [37]. In a study exploring the perception of survivors and their family as regards going back to school after the illness experience, participants expressed concerns with academic achievement because of those late effects [40]. According to survivors themselves, cognitive issues appeared gradually over time and resulted in academic challenges in the areas of memory, thought processing, organization and multi-tasking. However, although some neuropsychological domains are most consistently reported in the brain tumour survivors' literature, there exist no phenotype that encompasses all tumour types and treatments [36].

1.3.3 Psychosocial late effects

While not all psychosocial effects are negative (some cancer survivors report positive changes in life perspective, interpersonal relationships and within themselves) effects on long-term psychosocial functioning, including fears of recurrence, body image disturbances, poor emotional well-being, and anxiety and depression, have been reported. Indeed, survivors of childhood brain cancer, appear to report significantly higher global distress and depression scores than do their siblings [41] as well as anxiety and social isolation [42, 43]. A study by D'Agostino and Edelstein [44] attempting to identify the needs of young adult cancer survivors concluded that their singular and specific needs could be explained by their age and life stage. In a context of increasing expectations in school or at work, of making the achievement of typical developmental milestones, and of ongoing medical stressors as they grow older, the risk of psychological distress is higher for the adult with an history of cancer [12]. Concerns and challenges reported by survivors include dealing with their cognitive deficits, satisfaction with physical appearance, and changing life priorities [44].

1.3.4 Factors for late effects

Many factors have been identified through the years to explain the emergence of the variety of late effects, as can be seen in Figure 1.

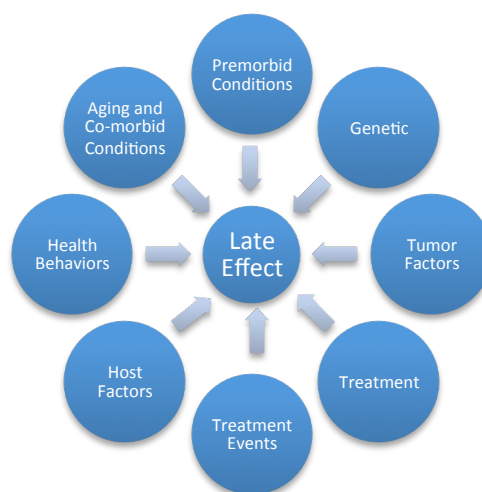


Figure 1.1
Factors for Late Effects

For example, the child's genetic, cancer diagnosis, age at diagnosis, tumour location, type of treatment received, and complications during treatment are factors of major importance for which late effects occur [45]. Treatment is one of the most important factors; research has shown a strong association between treatment exposure and late effects in this field [16]. Depending on the location of the tumour and the types of treatments used, tumour-directed interventions can greatly affect the developing central nervous systems of children and increase survivors' risk for long-term, treatment-related sequels that often worsen over time. The young brain being especially vulnerable, radiation during the first 3-5 years of life results in more important cognitive and neuropsychological late effects [46, 47]. Reports have shown that radiation therapy at a young age is the single most important factor for a poor functional outcome [48, 49], more than tumour location and histological diagnosis. Furthermore, young age at diagnosis is the strongest predictor of weakness and poor fitness [25]. Gender is another significant factor; women who survive childhood cancer have a greater risk of diminished health status [50], second cancers [51, 52], anthracycline-related cardiomyopathy and congestive heart failure [53], as well as cranial radiotherapy-related cognitive dysfunction, growth hormone deficiency, and obesity [54-56].

1.4 Health-related quality of life

Recently, the focus of research has shifted towards cancer's longer-term physical and psychosocial effects. The impact of cancer on quality of life (QoL) has therefore been increasingly documented [57-60]. Generic QoL describes general aspects of psychosocial and physical function such as

physical activity, self-concept, social relations and autonomy. Langeveld and others [61] reported that among young adult survivors of childhood cancer, many survivors reported being in good health and that most were functioning well psychologically. Other studies suggest that long-term consequences of cancer include issues present after diagnosis and treatment that linger, but also new concerns that develop over time [62]. A diagnosis of BT is a known risk factor for a decrease in quality of life when compared with other cancer survivors or healthy peers [63]. *Fatigue, aches, and pain* have all been symptoms reported by survivors that affected negatively their quality of life [64]. In the CCSS cohort, survivors were five more times more likely to report impaired QoL than were their siblings [65]. However, QOL appears to be a broad and idiosyncratic construct affected only moderately by health [66]. In order to assess how an individual's well-being may be affected over time by a disease, disability, or disorder, the concept of health-related quality of life (HRQoL) seems more appropriate.

Health-related QoL (HRQoL) is a multidimensional construct that refers to the perceived satisfaction in various health-related domains of life and includes at least physical, psychological, and social functioning [67, 68]. It is concerned with the impact of disease and treatment on daily functioning and the impact of perceived health on an individual's ability to live a fulfilling life. As survival rates increase, reducing treatment-related morbidity is a new challenge in oncology, and HRQoL has been found to be a useful construct to measure overall morbidity. It has emerged as an important health outcome in pediatric clinical trials and in strategies to improve clinical outcomes [69, 70]. Many of the morbidities associated

with childhood cancer survivorship have been shown to impact HRQoL, including organ damage, cognitive impairments, and psychosocial dysfunction [49, 71, 72]. In a study looking at the long-term psychosocial outcome of survivors, it was found that the brain tumour survivors have the poorest HRQoL among childhood survivors secondary to the tumour and its effects on the surrounding nervous tissue itself, to elevated intracranial pressure and impaired perfusion, and also to a complex array of treatment-related late effects [73]. Thus far, studies of HRQoL among BT survivors are not consistent across all types of brain tumours, including high-grade tumours such as medulloblastoma [74-76], low-grade tumours such as pilocytic astrocytoma [77-79] and mixed diagnosis [49, 80]. One explanation for this inconsistency is the heterogeneity of the diagnoses and treatment modalities.

Wilson and Cleary's model for health-related quality of life is a useful model to link clinical variables with HRQoL [81]. This model proposes a causal pathway model to link the field of objective measurement to that of subjective experience as can be seen in Figure 2. According to this model, the malfunction of any biological system generates various symptoms. Those symptoms experienced by survivors impact on their functional status. For example, malfunction of the endocrine system will generate fatigue, which will impact on the level of energy required to have a full-time job. The perception the survivor has of his or her own health and functioning will, in turn, impact on his or her subjective quality of life. The characteristics of the individual (age, gender, diagnosis) and of the environment (social support, medical care) influence all other variables.

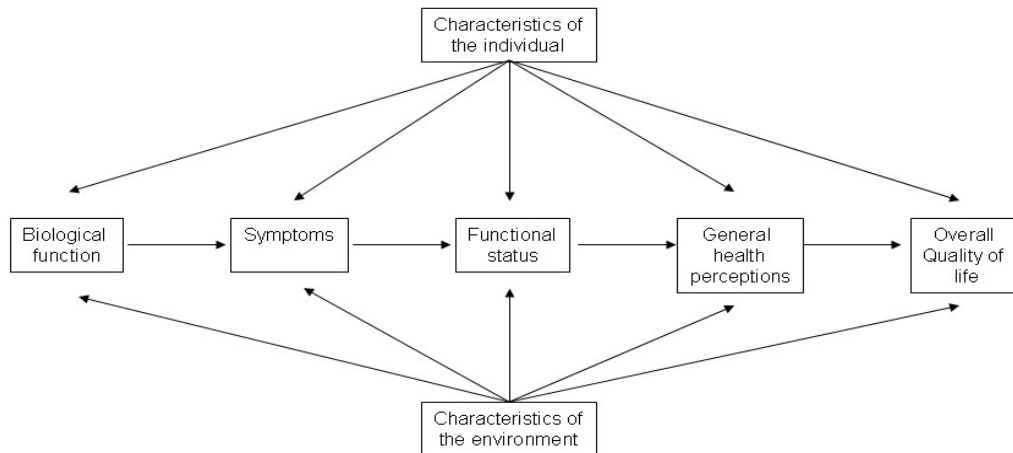


Figure 1.2
Wilson and Cleary Model

1.5 Functional Impact of Late Effects

Among cancer survivors, BT survivors are the group most likely to be functionally impaired [25, 27, 82]. Survivors are left to struggle with a host of issues including late effects in many domains that often leave them unnecessarily disabled or, at the very least, only able to function at a level that is not optimal. The late effects have a significant impact on BT survivors' life by impairing academic, vocational, and psychological functioning [14]. Survivors will have effects that influence their success, effort, and satisfaction in personal and vocational pursuits [83]. Less than an optimal function in the physical and cognitive domains may influence activities of daily living and greatly affect a survivor's ability to participate fully in expected roles at home, school, and work [25]. The combination of the various late effects often leaves survivors unable to manage their complex health problems independently and to function in society autonomously [84, 85]. In fact, BT survivors show decreased employment, less education beyond high school, and are less likely to live independently [25]. Indeed, according to CCSS, compared to siblings,

adult survivors are 23% more likely to use special education services, 4 times more likely to be unemployed, 20% less likely to marry, and more than twice as likely to live dependently [27, 85]. It has also been reported that 57% percent of children with brain tumours presented an academic deficit, and more specifically, arithmetic deficits were identified in 3 out of every 4 such children [86]. The ability of maintaining employment as adults was also found to be affected, as a study reported that only 54,5% of central nervous system (CNS) cancer survivors, which include brain tumours, were actively maintaining employment when interviewed after the age of 30, in contrast to 86,1% of survivors of childhood cancer that did not involve the CNS [87]. Common challenges reported by brain tumour survivors themselves in a study on identifying the needs of young adult cancer survivors included limited career options, poor social skills, and loss of autonomy [44]. Consequently, Eiser [88] emphasizes the challenge survivors have in balance between obtaining their “normalcy” while recognizing and living with the consequences of the disease after treatment.

1.6 Activities of Daily Living

The impact of late effects from oncology treatment on the survivors’ performance in daily living activities (ADL) are poorly quantified in the literature. Furthermore, reports regarding long-term follow-up of late effects using explicit measures of ADL ability are inexistent, with only one study addressing ADL performance using a self-report questionnaire [82]. Most of these reports employ HRQoL or sociodemographic indicators such as education achieved, insurability, employability, and marriageability

to represent “function” [15, 26, 35, 89], but this is a practice that leads to conflicting results. The use of self-report questionnaire or instruments based on broad functional classifications is contributing to the confusion and contradictions around functional status. Their ambiguity results from many factors: known shortcomings of such instruments, potential for respondents to unintentionally inflate their own functional status, and lack of specificity in scales employing broad categories of function to describe daily performance [90]. Unreliable results in self-reported outcomes by BT survivors can be explained by mild or severe cognitive deficits, short-term memory problems, or lack of self-awareness. A study by Smith and others [91] has found that self-reported physical function and performance status is often inaccurate in survivors of childhood cancer and that self-perception should be weighed carefully. There is an inconsistency in the results of these studies that is plainly linked to methodological shortcomings and, specifically, to the current state of functional outcome measurement in paediatric cancer survivors [90]. The measurement of functional ability and deficits is only as valid as the instruments used to measure the ability. Generic instruments, self-reports, and other commonly used tools lack accuracy in measuring actual ADL ability. Using narrower, standardized and observation-based assessment is likely to produce more accurate, real-life information on the functional status of survivors, particularly when the ability to self-report functional status accurately is questionable. Furthermore, having an accurate and detailed description of a patient’s ability is needed for professionals to design programs and interventions that aim to improve survivors’ functional outcome.

1.7 Oncology Rehabilitation

A multidisciplinary approach to the complex healthcare needs of childhood cancer survivors has been proposed as an efficient way to deliver care that is beneficial to patients, providers, and institutions [93]. Despite being so critical, oncology rehabilitation is an underdeveloped part of cancer care. Indeed, rehabilitation services are not a common aspect of survivorship health care as few cancer centers or hospitals offer comprehensive interdisciplinary oncology rehabilitation services [94], and thus the concept of oncology-specific rehabilitation is not well integrated in either oncology or rehabilitation culture. Rehabilitation and other allied healthcare professionals should be viewed as essential members of the multidisciplinary team in oncology, in particular in order to optimize functional outcomes. For example, survivors with performance limitations could benefit from intervention services to restore functional capacities, instruction in adaptive techniques to restore independent task performance, the provision of environmental adaptations to optimize participation, or from lifestyle interventions to optimize health and prevent further loss function [94]. However, according to a study on oncology rehabilitation, even institutions that have a major commitment to creating survivorship services may leave out or implement fragmented oncology rehabilitation services when they put together their survivorship program [95]. Furthermore, the outpatient rehabilitation needs of cancer survivors are often the most underserved, with one study demonstrating that patients are approximately 100 times more likely to receive rehabilitation care as an inpatient than as a outpatient [95]. Thus, during the acute phase of the illness, cancer patients are likely to receive rehabilitation services. However, this is not the case for the subsequent phases, after

the end of treatment or during the follow-up. This also means that cancer patients are likely to have rehabilitation services when they are hospitalized, but the patients who don't require hospitalisation might not have their rehabilitation needs addressed at all. A 2011 supplement issue of the American Journal of Physical Medicine Rehabilitations was duly dedicated to Cancer Rehabilitation, and the message across all articles was clear: it is urgent to direct our research efforts towards the building of evidence-based programs for cancer rehabilitation. Without the implementation of a rehabilitation program, it is possible that many children who experience deficits following paediatric brain tumour diagnosis and treatment do not receive the services they need to optimize their development. This can result in limitations for survivors that could have been either prevented or improved with rehabilitation. A major challenge within paediatric oncology is therefore to sustain the high survival rates while striving to achieve optimal quality of life [96-98] as well as functional outcome. To attain this goal, rehabilitation is essential.

CHAPTER 2: RATIONALE, OBJECTIVES, AND HYPOTHESES

2.1 Rationale

A new goal in the area of cancer research is to extend the horizon of the success of childhood cancer treatment beyond 5-year survival to a life free of disability and disease. Improvement in oncology diagnosis and treatments has increased the survival rate to approximately 70% for children with brain tumours [13], consequently elevating the importance of considering the late effects, quality of life, and functional outcomes in survivors. Childhood cancer survivors are left to struggle with late effects from their cancer and the treatments received, and brain tumour (BT) survivors are among the groups most likely to be functionally impaired [25, 27, 82]. However, little is known about the impact of late effects from oncology treatment on the survivors' performance in daily living activities (ADL). Long-term late effects have been extensively studied from a medical point of view, but very little from a rehabilitation perspective. Furthermore, research studies in BT survivors using explicit measures of ADL ability are nonexistent, as most studies use self-report questionnaires to gather information about functional outcome. In order to design interventions to improve the functional outcome of the survivors, there is a need to use measures that provide information on the quality of performance and on the type of performance skills that are problematic. Moreover, to understand the impact of cancer on the life of survivors from their perspective, health-related quality of life (HRQoL) is recognized as an important health outcome [99]. However, the relationship between

functional outcome and HRQoL in BT survivors has not been investigated yet.

2.2 Objectives

The purpose of this study is to produce new knowledge about childhood brain tumour survivors. This study evaluates the long-term impact of brain tumour and its treatment on the functional outcome, more specifically on performance in activities of daily living, and the health related quality of life in adolescent and young adult survivors. Furthermore, as research focusing on identification and characterization of high-risk populations is an essential foundation on which to build evidence-based recommendations for long-term follow-up, this study also aims to identify factors that are likely to be associated with performance limitations.

The primary objective was to estimate the extent to which young adult survivors of childhood brain tumour achieve a level of performance in activity of daily living that is comparable to their peers, 5 years after diagnosis. The secondary objectives were:

- 1) to assess the association between observed limitations in motor and process skills and the HRQoL of BT survivors;
- 2) to determine which personal and clinical factors are likely to be associated with performance limitations, including age at diagnosis, time since treatment, gender, tumour type and location, type of treatment and chronic health conditions.

2.3 Hypotheses

The following hypotheses were examined:

1) For the primary objective, it is expected that motor and process skills of the BT survivors, as evaluated by the AMPS, will be significantly lower than the age norms.

2) For the secondary objectives, it is expected that:

- childhood BT survivors experience functional impairments that affect their HRQoL. Therefore, their HRQoL will be associated with the level of performance in both the mental or physical subscale of the SF-12 questionnaire. Moreover, it is expected that the HRQoL will be significantly lower than the population norms for both subscales.
- based on the literature, younger age at diagnosis and higher dose of radiation are expected to be factors associated with low level of function.

CHAPTER 3: Long term effects of childhood brain tumour on functional outcome of survivors

Catherine Demers^{1,2}, B.Sc., Isabelle G  linas^{1,3}, Ph.D., Anne-Sophie Carret², MD.

¹School of Physical and Occupational Therapy, McGill University,
Montreal, Quebec, Canada

²Division of Haematology-Oncology, CHU Ste-Justine, Montreal, Quebec,
Canada

³Montreal Center for Interdisciplinary Research in Rehabilitation (CRIR)-
Jewish Rehabilitation Hospital research site, Laval, Quebec, Canada

Manuscript prepared for the submission to *Pediatric Blood and Cancer*

Running Title: Functional outcome in brain tumour survivors

Mailing address: Isabelle G  linas

School of Physical and Occupational Therapy,
Faculty of Medicine, McGill University
3654 Drummond Street,
Montreal, Quebec,
Canada, H3G 1Y5

Isabelle.gelinas@mcgill.ca

3.1 ABSTRACT

Background. Long-term side effects of treatment in paediatric BT are known. However, their impact on performance in activities of daily living (ADL) in young survivors and the variables associated with the level of performance has yet to be documented. **Procedure.** Performance in ADL of paediatric BT survivors was measured by the Assessment of Motor and Process Skills (AMPS) assessment ≥ 5 years after diagnosis. Socio-demographic and medical information were also collected. **Results.** Thirty-six young adults, mean age 21.0 years (range 16-29), mean time since completion of treatment 10.1 years (4.0-18.0), participated in this study. Results showed that 55% of the participants had results under the motor cut-off and 36% under both the motor and process cut-off representing the lower limit of competent ADL task performance, meaning they demonstrate increased effort or inefficiencies, safety risks, and need for assistance when performing ADL tasks in general. Lower level of functioning was associated with younger age at diagnosis and multiple chronic health conditions for process skills; and tumour type, longer time since treatment and multiple chronic health conditions for motor skills. **Conclusion.** Five years or more after diagnosis, young adults survivors of childhood BT show decreased motor and process skills affecting their performance in ADL. Rehabilitation and prevention programs should therefore be developed to optimize their functional outcome. Patients at heightened risk should be particularly targeted for follow-up.

Keywords: paediatric brain tumour; paediatric brain tumour survivors; functional outcome; activities of daily living; late effects

3.2 INTRODUCTION

The survival rate of brain tumour (BT) in children has increased significantly with the advancement in diagnoses and treatment (Howlader et al., 2011). In North America, it is estimated that approximately 70% of children are survivors, 5 years after diagnosis (American Cancer Society, 2009; Canadian Cancer Society, 2011). This success has brought a need to consider the functional outcome and quality of life of the survivors. Hence, the tumour itself, the surgery and the treatment, including radiation therapy and chemotherapy, generate a variety of late effects that can often be chronic. The term late effect refers to a late-occurring or chronic outcome, either physical or psychological, that persists or develops beyond 5 years from diagnosis and that is produced by the use of cancer therapy at an early age (Neglia et al., 2001) or the disease process. The wide array of late effects affects the whole person and includes physical, sensory, cognitive, neurological, and endocrine complications (Armstrong, 2010). Therefore, the research focus in oncology has recently shifted toward the long-term side effects of cancer and its treatment.

The emergence of late effects depends on many factors, including genetic, treatment received and type of tumour. Treatment is one of the most important factors; research has shown a strong association between treatment exposure and late effects in this field (Oeffinger et al., 2006). Reports have shown that radiation therapy of the CNS at a young age is the single most important factor for a poor functional outcome (Merchant et al., 2009; Reimers, et al., 2009), more than tumour location and histological diagnosis.

Cancer during childhood can become a lifelong problem, compromising the individual's capacity to meet developmental expectations across a range of functional domains. Various studies have shown impairment in motor, cognitive, and functional performance after the completion of treatment. For example, chemotherapy agents such as vincristine can cause neuropathy, cranial radiation therapy generates neurocognitive effects, and surgery can be responsible for neurological deficits. Less than optimal function in physical and cognitive domains may influence performance in activities of daily living and greatly affect a survivor's ability to fully participate in expected roles at home, school, and work (Ness et al., 2010). The combination of the various late effects often leaves survivors unable to manage their complex health problems independently and to function autonomously in society (Gurney et al., 2009; Pang et al., 2008). In fact, BT survivors show decreased employment, less education beyond high school, and are less likely to live independently (Ness et al., 2010). The impact on the everyday living and the performance in daily activities is, however, poorly quantified in the literature. Information on the quality of performance and the performance skills that are problematic is important for clinical practice so that programs and interventions can be designed to meet the specific needs of survivors.

Therefore, the aim of our study was to assess the impact of late effects of childhood brain tumour and related treatment on the performance in daily living activities of survivors. Furthermore, we wanted to determine which factors are likely to be associated with performance limitation.

3.3 METHODS

Participants

Study participants were recruited from a long-term follow-up clinic at a major paediatric university hospital, the CHU Ste-Justine, in Montreal. Eligibility was restricted to survivors aged ≥ 16 years, who were treated for BT at CHU Ste-Justine between 1987 and 2007 when ≤ 21 years of age, were at least 3-years post end of treatment, 5 years post diagnosis, with brain tumour as their first cancer occurrence. Individuals who had tumour located in the spinal cord, who were treated only by surgery, or who had a pre-existing comorbid condition not related to the cancer that might affect the functional outcome were not eligible. Participants had to complete a socio-demographic as well as a health-related quality of life questionnaire, and a functional measure, the Assessment of Motor and Process Skills (AMPS) was administered. A convenience sample of 36 participants was recruited.

The Research Ethics Board of CHU Ste-Justine approved the study protocol. Written informed consent was obtained from participants ≥ 18 years old and from parents for participants < 18 years old.

Exposures

Socio-demographic and medical data were collected from the participants' medical chart. The following factors were collected and considered in the analysis: age at diagnosis (< 7 or ≥ 7 years), gender (male or female), time since treatment (< 10 or ≥ 10 years), tumour type (medulloblastoma or PNET; glioma or astrocytoma; other), tumour location (posterior fossa; parasellar or supratentorial), treatment type (no radiation or cranial

radiation; craniospinal radiation), dose of radiation ($<55\text{Gy}$ or $\geq 55\text{Gy}$), relapse (yes or no), and chronic health condition (0, 1 or 2 and more). Age at diagnosis was dichotomized at 7 years for comparison with previous studies (Hjern, Lindblad, & Boman, 2007; Schreiber et al., 2014). The number of chronic health conditions was counted as the number of system affected by late effects in the following: endocrine, musculoskeletal, neurological or neurosensory, other. A socio-demographic questionnaire designed for this study was used to collect the following functional variables: level of education according to the highest degree (elementary school, high school, cegep or professional school, university), occupation (studying or working full-time; studying in special program or sheltered employment or working part-time; unemployed), and level of autonomy (living independently or not). Living independently refers to living alone, with partner, or roommates.

Outcome

In order to assess the performance in activities of daily living (ADL) of BT survivors, a standardized objective measure, the Assessment of Motor and Process Skills (AMPS) (Fisher, 2010), was used. The AMPS is an observational assessment, used to measure the quality of task performance in the context of familiar and relevant tasks. During an AMPS evaluation, the quality of 16 ADL motor and 20 ADL process skills is assessed while the participants perform two tasks of their choice from the list of calibrated AMPS tasks, such as making a sandwich or vacuuming a small room. ADL motor skills are observable actions a person performs in order to move oneself and task objects while interacting with task object and environment during an ADL task (e.g. “reaches”, “bends” and

“calibrates”). ADL process skills are observable actions a person enacts when (a) selecting, interacting with, and using task tools and materials; (b) carrying out individual actions and steps; and (c) modifying task performance when problems are encountered (e.g. “initiates”, “notifies and responds” and “organizes”). Of note that motor and process skills as evaluated by the AMPS are goal-directed actions, they are not physical or cognitive capacities, such as range of motion or memory. The assessments were administered to study participants by the main researcher, who was trained in its use and calibrated with demonstrated rater reliability. The AMPS has been standardized on over 125,000 clients worldwide. Studies support the reliability and validity of the AMPS across age groups and gender (Hayase et al., 2004; Merritt & Fisher, 2003) and its sensitivity as an outcome measure has also been demonstrated (Cooke et al., 2000; Graff et al., 2006; Kottorp, Bernspang, & Fisher, 2003). The AMPS has been used in a study evaluating the ADL performance of paediatric sarcoma survivors (Parks et al., 2009). The use of this evaluation allowed the research team to collect new and highly relevant information in this population. Furthermore, the cut-off indicators established by the AMPS that represent the lower limit of competent ADL task performance can be used to divide into two groups the participants in regard to their level of performance. Clients with ability measures below the cut-off measure on the ADL motor scale are likely to demonstrate increased effort when performing ADL tasks in general. Clients with ability measures below the cut-off measure on the ADL process scale are likely to demonstrate increased inefficiencies, safety risks, and need for assistance when performing ADL tasks in general. In addition, clients below the cut-off measure on the ADL process scale are likely to need

assistance to function in community (Fisher, 2010).

Statistical approach

Descriptive statistics and frequency distributions were generated (mean, SD, %) for the personal and clinical characteristics to describe the study participants. AMPS computer-scoring software was used to generate ADL motor and ADL process ability measures for each study participant. This program uses many-faceted Rasch analysis to convert the raw, ordinal ADL motor and ADL process skills scores to linear ADL motor and ADL process ability measures expressed in equal-interval, log odds probability units, termed “logits”. The scores were dichotomized using the AMPS cut-off: scores below the cut-off measure were defined as having a low level of performance. Then, we compared the personal and medical characteristics of the survivors according to their level of performance in process and motor skills. Furthermore, the level of education, occupation, and independence status were compared between survivors with limitation in motor and process skills and those without using chi-square statistics.

To determine which personal and medical factors are likely to be associated with performance limitation, univariate logistic regression was used to evaluate the strength of their associations (odds ratio [OR] with corresponding 95% confidence interval [CI]) between survivors with or without limitation in motor and process skills. Univariate logistic regressions were performed with all potential variables against each of the outcome variables. Data analysis was performed using SPSS version 20.

3.4 RESULTS

Characteristics of the study population

Thirty-six brain tumour survivors participated in this study. The average age of the participants was 21.0 years with a range between 16 and 29 years. There were more females (63,9%) than males. The most common type of tumor was Medulloblastoma or PNET (63,9%). The age at diagnosis ranged from 0 to 19 years. Sixty-seven percent of the participants received craniospinal radiation as opposed to only cranial (19,4%) or no radiation (2,8%). The majority were studying (regular or special program) or working either in sheltered program or part-time (55.6%) and were living with family or in a resource (80.6%). Table I shows the personal and medical characteristics of the participants for the whole group as well as for subgroups according to the level of performance for the process and motor skills (low vs high level).

ADL performance

Using the cut-off indicators established by the AMPS that represent the lower limit of competent ADL task performance, 20 participants (55%) had a performance under the motor cut-off and 13 (36%) under the process cut-off. The 13 participants with results under the process cut-off also had a score under the cut-off for motor skills. Therefore, 36% of the participants demonstrated increased effort and inefficiencies, safety risks, and need for assistance when performing ADL tasks in general. For example, a significant number of participants showed ineffective pacing skill that was observed by a task performed at a slow rate or that gradually becomes slower as task progress. Another example is an ineffective noticing/responding skill that disrupts the task performance, such as a

delay before turning a burner or the water off. Furthermore, as shown in Table 2, there is a significant difference for the level of education, the occupation, and the independence status between survivors under and above the motor cut-off; and a significant difference for the level of education and the occupation when considering the process cut-off.

Factors associated with performance limitation

The results of the logistic regression models that were designed to evaluate associations between ADL performance and personal characteristics and clinical variables are provided in Table 3. Gender (OR 0,19; 95% CI 0,04-0,85), time since treatment (OR 0,2; 95% CI 0,05-0,08), tumour location (OR 9,0; 95% CI 1,97-41,08), chronic health conditions (OR 0,06; 95%CI 0,01-0,51) were found to be associated with performance in motor skills. As for the process skills, age at diagnosis (OR 7,6; CI 1,609-35,906) was the only factor found to be significantly associated with the level of performance. Tumour type, treatment type, relapse, and dose of radiation were also assessed but were not found to have a significant association with ADL motor or process skills performance.

3.5 DISCUSSION

The purpose of this study was to examine the ADL functioning of a group of BT survivors using an objective, well-standardized performance-based assessment. The study showed that the ADL functioning of BT survivors was affected, with about half of the participants under the motor performance cut-off and a third under both the process and motor cut-offs, suggesting more physical effort and less efficiency while performing ADLs.

Furthermore, these results suggest that the BT survivors are less likely to be safe and/or independent when living in the community. To our knowledge, this study is the first to assess the skills of functional independence from an objective perspective. Other studies investigating independence in ADLs used questionnaire asking about the survivors' current living situation (Bhat et al., 2005; Ness et al., 2005). However, even though it is an indicator of independence, living with family does not imply necessarily that the young adults have the skills to be independent or safe and living alone does not give us information on how the young adults are managing their responsibilities and if they receive help. Our results from the AMPS assessment provide novel information on how the participants are performing their ADLs, not only information on what they can or cannot do.

According to the AMPS, the process skills are a stronger indicator of participation and of independent living than motor skills (Fisher, 2010). However, in this cohort, all the participants who had limitation in process skills also had limitations in motor skills. It is therefore difficult to isolate the impact and contribution of each type of limitation. Regarding the occupation, few participants were unemployed or not attending school, however they reported how difficult it was for them to find a job that corresponds to their capacities or limitations and meets their professional aspiration at the same time. Moreover, the participants with limitations in ADL performance were also more likely to be enrolled in a special education program or to work in a sheltered job than to work or study in the regular system. Consistent with previous research (Mitby et al., 2003), BT survivors in this study demonstrated lower level of academic

achievement, when compared to the Canadian statistics (Statistic Canada, 2012). Indeed, participants were more likely to have no degree or diploma (36,1% in this cohort compared to 19,1%) and less likely to graduate from university (8,4% vs 22,2%). Furthermore, participants with limitations in ADL performance were less likely than those without to graduate from high school.

This study allowed us to identify several factors that are likely to be associated with specific performance limitations. According to the studies of Mulhern (2001) and Ris (2001) receiving cranial radiation at a young age greatly increases the risk for developing neurocognitive late effects across several domains of functioning. Our findings supported the assumption that lower age at diagnosis is a factor associated with low level of function, but in process skills only. This result is consistent with the literature on neuropsychological late effects. Neurocognitive dysfunction is a known complication associated with radiation therapy, which may affect the process skills necessary while performing a functional task. For example, participants showed decreased processing speed and limited attention span that interfered with task progression. However, because only one participant did not receive radiation, it was not possible to assess its specific effect. The dose and type of radiation were not significantly associated with level of performance in our study.

Because having multiple chronic health conditions was associated with motor skills outcome, the BT patients who develop late effects in many domains should be closely followed-up by the health care system. Longer time since treatment was also associated with low level of function, which

emphasizes the fact that late effects are chronic conditions and can worsen over time. Moreover, it means that the functional impact of late effects can also be more important over time. The transition from childhood to adulthood is characterised by the development of identity and separation from the nuclear family. Young adults typically have to focus on independent living, intimate relationships, attending college, and pursuing vocational goals. This transition is especially complicated for cancer survivors dealing with late effects as the requirements and expectations in school, work, and society are higher which confronts them to a greater extent to their difficulties. The medical and rehabilitation long-term follow-up is therefore crucial. The last variable associated with motor performance was tumour location; participants with a tumour located in the posterior fossa were more likely to present a low level of function than other location in the brain. This result can be explained by the location of the posterior fossa near the brainstem and cerebellum, which are the parts of the brain responsible for movement, balance, and coordination. Finally, consistent with the results of other studies on health status and medical late effects of cancer survivors (Hudson et al., 2003; Lipshultz et al., 1995), female gender is another significant factor for a poor outcome in motor skills in our study.

Study limitations

Interpretation of our results must take into account potential study limitations. The small number of subjects available for this study made it difficult to have a homogeneous group and provided limited power to detect important size differences in mean scores between subgroups.

Furthermore, the study design (cross-sectional) only provides a snapshot of the situation and makes it difficult to make causal inference. Other limitations are the absence of proper control group and the restriction of the data to one hospital, which may limit the generalizability of the results.

Conclusion

Results from this study underline the significance of the impact of childhood BT and related treatments on the functional outcome of survivors. A significant proportion of adult survivors of childhood BT demonstrated increased effort and inefficiencies, safety risks, and need for assistance when performing ADL tasks. Furthermore, in an effort to identify factors predicting an unfavourable functional outcome, the AMPS scores were compared with personal and clinical factors. Young age at diagnosis was found to be associated with poor functional outcome in process skills. For the motor skills, gender, longer time since treatment, tumour location, and multiple chronic health conditions were associated with poor functional outcome.

The goal of the management of brain tumour should be long-term progression-free survival with minimal morbidity and optimal function. In this context, rehabilitation services should be considered as mandatory, especially for the more vulnerable subgroups. Moreover, the study of long-term outcomes among brain tumour survivors reflects an excellent opportunity to assess a variety of treatment approaches that will optimise their functional outcome and independence in ADL as well as enhance the opportunity to live a fulfilling life. As new protocols and new radiation

techniques such as proton therapy are being developed in order to reduce the adverse effects of therapy, it will be interesting to compare these results with the new cohorts of survivors. Future studies of outcome in childhood brain tumour should include not only assessment of tumour control and of neurological and endocrine complications, but also the impact of the tumour and its treatment on function with the use of exhaustive qualitative and quantitative measures.

Acknowledgments

This research was supported by the Coast-to-Coast Foundation. We would like to acknowledge the contribution of the oncology rehabilitation team of Ste-Justine Hospital and to thank the participants for their very precious time and generosity.

TABLES

Table 3.1 Characteristics of the Study Participants (n= 36) *mean(SD) or N(%)*

Characteristics	Total n=36	Low process n=13	High process n=23	Low motor n=20	High motor n=16
	Mean (SD)	Mean (SD)		Mean (SD)	
Age at evaluation (years)	21,0 (3,3)	20,2 (2,3)	21,48 (3,7)	21,3 (3,4)	20,69 (3,3)
Time since end of treatment (years)	10,1 (3,8)	12,0 (3,6)	10,43 (5,0)	11,7 (3,5)	11,0 (4,5)
Age at diagnosis (years)	8,9 (5,1)	6,3 (4,3)	9,0 (3,6)	7,3 (5,0)	8,1 (3,3)
	N (%)	N (%)		N (%)	
Gender					
Female	22 (61,1)	8 (61,5)	14 (60,9)	15 (75,0)	7 (43,8)
Male	14 (38,8)	5 (38,5)	9 (39,1)	5 (25,0)	9 (56,3)
Tumour type					
Medulloblastoma or	21 (58,3)	8 (61,5)	13 (56,5)	14 (70,0)	7 (43,8)
PNET	4 (11,1)	2 (15,4)	3 (13,0)	3 (15,0)	2 (12,5)
Astrocytoma or glioma	11 (30,6)	3 (15,4)	7 (30,4)	3 (15,0)	7 (43,8)
Other					
Tumour location					
Posterior fossa	22 (61,1)	8 (61,5)	13 (56,5)	15 (75,0)	6 (37,5)
Supratentorial or parasellar	14 (38,9)	5 (38,5)	10 (43,4)	5 (25,0)	10 (62,5)
Type of treatment					
No radiation	1 (2,8)	0 (0)	1 (4,3)	0 (0)	1 (6,3)
Cranial radiation	11 (30,1)	1 (7,7)	4 (17,3)	3 (15,0)	2 (12,5)
Cranial and spinal radiation	24 (66,6)	12 (92,3)	18 (78,3)	17 (85,0)	13 (81,2)
Radiation dose					
<55Gy	16 (44,5)	6 (46,2)	12 (52,2)	7 (35,0)	11 (68,8)
≥55Gy	18 (55,5)	7 (53,8)	11 (47,8)	13 (65,0)	5 (31,2)
Chronic health conditions†					
0	3 (8,4)	0 (0)	3 (13,0)	0	3 (18,8)
1	7 (19,4)	1 (7,7)	6 (26,1)	1 (5,0)	6 (37,5)
≥2	26 (72,2)	12 (92,3)	14 (60,9)	19 (95,0)	7 (43,8)
Rehabilitation Services					
Occupational Therapy	24 (66,7)	-	-	-	-
Physiotherapy	27 (75,0)				
Psychology	24 (66,7)				
Speech Therapy	4 (11,1)				

Table 3.2 Functional characteristics of the study participants (n= 36)
N(%)

Characteristics	Total n=36	Low process n=13	High process n=23	Low motor n=20	High motor n=16
	N (%)	N (%)		N (%)	
Level of education (highest diploma) *†					
Elementary school	13 (36,1)	1 (7,7)	3 (13,0)	11 (55,0)	2 (12,5)
High school	9 (25,0)	10 (76,9)	4 (17,4)	6 (30,0)	3 (18,8)
Cegep or professional school	11 (13,9)	2 (15,4)	6 (26,1)	2 (10,0)	9 (56,3)
University	3 (8,4)	0 (0)	3 (13,0)	1 (5,0)	2 (12,5)
Occupation*†					
Studying or working full-time	20 (55,6)	3 (23,1)	17 (73,9)	7 (35,0)	13 (81,2)
Studying special program, sheltered employment or part-time	13 (36,1) 3 (8,3)	9 (69,2)	4 (17,4)	11 (55,0)	2 (12,5)
Unemployed		1 (7,7)	2 (8,7)	2 (10,0)	1 (6,3)
Independence status†					
Independent	29 (80,6)	1 (7,7)	5 (21,7)	1 (5,0)	5 (31,2)
Living with family or in resource	7 (19,4)	12 (92,3)	18 (78,3)	19 (95,0)	11 (68,8)

* Significant difference between low process and high process ($p < 0.05$)

† Significant difference between low motor and high motor ($p < 0.05$)

Table 3.3 Association between motor and process skills and clinical characteristics (n=36)

Characteristics	Motor skills		Process skills	
	OR	95% CI	OR	95% CI
Gender	5.143*	1.176-22.483	1.446	0.341-6.136
Age at diagnosis	3.545	0.765-16.433	7.6*	1.609-35.906
Time since treatment	0.2*	0.048-0.837	0.275	0.060-1.267
Tumor type	2.464	0.732-8.291	1.451	0.455-4.629
Tumor location	9.0*	1.972-41.075	1.747	0.437-6.972
Treatment type	0.388	0.077-1.963	1.080	0.212-5.949
Dose of radiation	0.372	0.094-1.472	1.467	0.367-5.858
Relapse	0.571	0.091-3.608	0.5	0.085-2.939
Chronic health conditions	0.057*	0.006-0.515	0.163	0.021- 1.266

Note: OR = Odds ratio; CI = confidence interval; *significant p<0.05

REFERENCE LIST

- American Cancer Society (2009). *Cancer Facts & Figure 2009*. Atlanta, GA: American Cancer Society.
- Armstrong, G. T. (2010). Long-term survivors of childhood central nervous system malignancies: the experience of the Childhood Cancer Survivor Study. *Eur J Paediatr Neurol*, 14(4), 298-303.
- Bhat, S. R., Goodwin, T. L., Burwinkle, T. M., Lansdale, M. F., Dahl, G. V., Huhn, S. L., Fisher, P. G. (2005). Profile of daily life in children with brain tumors: an assessment of health-related quality of life. *J Clin Oncol*, 23(24), 5493-5500.
- Canadian Cancer Society (2011). *Canadian Cancer Statistics 2011*. Toronto, ON: Canadian Cancer Society's Advisory Committee on Cancer Statistics.
- Cooke KZ, F. A., Mayberry W, et al. . (2000). Differences in activities of daily living process skills of persons with and without Alzheimer's disease. *Occup Ther J Res*, 20, 87-103.
- Fisher, A. G. (2010). *Assessment of motor and process skills*. Vol. 1: Development, standardization, and administration manual, 7th ed. Ft. Collins, CO: Three Star Press.
- Graff, M. J., Vernooij-Dassen, M. J., Thijssen, M., Dekker, J., Hoefnagels, W. H., & Rikkert, M. G. (2006). Community based occupational

- therapy for patients with dementia and their care givers: randomised controlled trial. *BMJ*, 333(7580), 1196.
- Gurney, J. G., Krull, K. R., Kadan-Lottick, N., Nicholson, H. S., Nathan, P. C., Zebrack, B., et al. (2009). Social outcomes in the Childhood Cancer Survivor Study cohort. *J Clin Oncol*, 27(14), 2390-2395.
- Hayase D, M. D., Thimmaiah D, et al. . (2004). Age-related changes in activities of daily living ability. *Aust Occup Ther J*, 51, 192-198.
- Hjern, A., Lindblad, F., & Boman, K. K. (2007). Disability in adult survivors of childhood cancer: a Swedish national cohort study. *J Clin Oncol*, 25(33), 5262-5266.
- Howlader, N. A., Krapcho M, et al. (2011). SEER Cancer Statistics Review, 1975-2008, from http://seer.cancer.gov/csr/1975_2008/
- Hudson, M. M., Mertens, A. C., Yasui, Y., Hobbie, W., Chen, H., Gurney, J. G., et al. (2003). Health status of adult long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. *JAMA*, 290(12), 1583-1592.
- Kottorp, A., Bernspang, B., & Fisher, A. G. (2003). Validity of a performance assessment of activities of daily living for people with developmental disabilities. *J Intellect Disabil Res*, 47(Pt 8), 597-605.
- Lipshultz, S. E., Lipsitz, S. R., Mone, S. M., Goorin, A. M., Sallan, S. E., Sanders, S. P., et al. (1995). Female sex and drug dose as risk factors for late cardiotoxic effects of doxorubicin therapy for childhood cancer. *N Engl J Med*, 332(26), 1738-1743.
- Merchant, T. E., Conklin, H. M., Wu, S., Lustig, R. H., & Xiong, X. (2009). Late effects of conformal radiation therapy for pediatric patients with low-grade glioma: prospective evaluation of cognitive, endocrine, and hearing deficits. *J Clin Oncol*, 27(22), 3691-3697.
- Merritt, B. K., & Fisher, A. G. (2003). Gender differences in the performance of activities of daily living. *Arch Phys Med Rehabil*, 84(12), 1872-1877.
- Mitby, P. A., Robison, L. L., Whitton, J. A., Zevon, M. A., Gibbs, I. C., Tersak, J. M., et al. (2003). Utilization of special education services and educational attainment among long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. *Cancer*, 97(4), 1115-1126.
- Mulhern, R. K., Palmer, S. L., Reddick, W. E., Glass, J. O., Kun, L. E., Taylor, J., et al. (2001). Risks of young age for selected neurocognitive deficits in medulloblastoma are associated with white matter loss. *J Clin Oncol*, 19(2), 472-479.

- Neglia, J. P., Friedman, D. L., Yasui, Y., Mertens, A. C., Hammond, S., Stovall, M., et al. (2001). Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study. *J Natl Cancer Inst*, 93(8), 618-629.
- Ness, K. K., Mertens, A. C., Hudson, M. M., Wall, M. M., Leisenring, W. M., Oeffinger, K. C., et al. (2005). Limitations on physical performance and daily activities among long-term survivors of childhood cancer. *Ann Intern Med*, 143(9), 639-647.
- Ness, K. K., Morris, E. B., Nolan, V. G., Howell, C. R., Gilchrist, L. S., Stovall, M., et al. (2010). Physical performance limitations among adult survivors of childhood brain tumors. *Cancer*, 116(12), 3034-3044.
- Oeffinger, K. C., Mertens, A. C., Sklar, C. A., Kawashima, T., Hudson, M. M., Meadows, A. T., et al. (2006). Chronic health conditions in adult survivors of childhood cancer. *N Engl J Med*, 355(15), 1572-1582.
- Pang, J. W., Friedman, D. L., Whitton, J. A., Stovall, M., Mertens, A. C., Robison, L. L., & Weiss, N. S. (2008). Employment status among adult survivors in the Childhood Cancer Survivor Study. *Pediatr Blood Cancer*, 50(1), 104-110.
- Parks, R., Rasch, E. K., Mansky, P. J., & Oakley, F. (2009). Differences in activities of daily living performance between long-term pediatric sarcoma survivors and a matched comparison group on standardized testing. *Pediatr Blood Cancer*, 53(4), 622-628.
- Reimers, T. S., Mortensen, E. L., Nysom, K., & Schmiegelow, K. (2009). Health-related quality of life in long-term survivors of childhood brain tumors. *Pediatr Blood Cancer*, 53(6), 1086-1091.
- Ris, M. D., Packer, R., Goldwein, J., Jones-Wallace, D., & Boyett, J. M. (2001). Intellectual outcome after reduced-dose radiation therapy plus adjuvant chemotherapy for medulloblastoma: a Children's Cancer Group study. *J Clin Oncol*, 19(15), 3470-3476.
- Schreiber, J. E., Gurney, J. G., Palmer, S. L., Bass, J. K., Wang, M., Chen, S., Gajjar, A. (2014). Examination of risk factors for intellectual and academic outcomes following treatment for pediatric medulloblastoma. *Neuro Oncol*.
- Statistics Canada (2012). *Labour force survey estimates (LFS), by educational attainment, sex and age group, annual (persons unless otherwise noted)*, Government of Canada, from : <http://www4.hrsdc.gc.ca/.3ndic.1t.4r@-eng.jsp?iid=29>

CHAPTER 4: INTEGRATION OF MANUSCRIPT

The first manuscript explored the association between the variables of the first part of the Wilson and Cleary Model, which are biological function, symptoms experienced by BT survivors, and functional status, considering the interaction of the characteristics of the individual and environment. It was done by assessing the level of performance in activities of daily living of BT survivors (low vs. high) and by evaluating its association with personal and medical factors. The second manuscript explores the second part of the model, which is the interaction between functional status, general health perceptions, and quality of life, always considering the characteristics of the individual and the environment. This manuscript explores the performance in activities of daily living in relation to the age norms, and evaluates its association with health related quality of life.

CHAPTER 5: Activities of Daily Living and Health Related Quality of Life in Survivors of Childhood Brain Tumour

Catherine Demers^{1,2}, B.Sc., Isabelle Gélinas^{1,3}, Ph.D., Anne-Sophie
Carret², MD.

¹School of Physical and Occupational Therapy, McGill University,
Montreal, Quebec, Canada

²Division of Haematology-Oncology, CHU Ste-Justine, Montreal, Quebec,
Canada

³Montreal Center for Interdisciplinary Research in Rehabilitation (CRIR)-
Jewish Rehabilitation Hospital research site, Laval, Quebec, Canada

Manuscript prepared for the submission to *American Journal of
Occupational Therapy*

Running Title: Activities of Daily Living in Survivors of Childhood Brain
Tumour

Mailing address: Isabelle Gélinas

School of Physical and Occupational Therapy,
Faculty of Medicine, McGill University
3654 Drummond Street,
Montreal, Quebec,
Canada, H3G 1Y5

Isabelle.gelinas@mcgill.ca

5.1 ABSTRACT

Objective. This cross-sectional, descriptive study compared the performance in activities of daily living of young adults survivors of childhood brain tumour (BT) with norms and explored associations with health-related quality of life (HRQoL). **Methods.** Thirty-six participants were examined using the AMPS, a standardized objective measure, to evaluate the quality of ADL task performance and the SF-12 questionnaire to evaluate the HRQoL. **Results.** The survivors had significantly lower performance in activities of daily living compared to the age norms ($p < 0.01$). Furthermore, functional level was found to be positively associated with the physical component scale ($r^2 = 0.5$) and the mental component scale ($r^2 = 0.3$) of the HRQoL. **Conclusion.** Late effects of treatment for childhood BT have a significant impact on the performance in activities of daily living in both motor and process skills. Recognition of the results from this study emphasizes the importance of the long-term follow-up of these patients as well as the rehabilitation services aiming at improving the functional level and HRQoL of survivors.

MeSH TERMS : brain tumour, paediatrics, functional outcome, activities of daily living, health-related quality of life

5.2 INTRODUCTION

Innovations in medical technology have led to advances in detection and improved treatment of cancers, thus increasing the survival rate to approximately 70% for children with brain tumours in North America (Jemal et al., 2003; Canadian Cancer Society, 2011). Nevertheless,

survivors are left to struggle with a host of issues including certain treatment related toxicities. Long-term deficits secondary to the tumour and its treatments may include physical, sensory, cognitive, neurologic, and endocrine complications. These late effects often leave the patients unnecessarily disabled or, at the very least, only able to function at a level that is not optimal (National Research Council, 2005). In children with brain tumours (BT), the percentage of survivors with a medium, high, or severe burden score of adverse events is estimated at more than 80% (Geenen et al., 2007) and 60% have at least one impairment (Aarsen et al., 2006; Macedoni-Luksic, Jereb, & Todorovski, 2003).

Furthermore, a study reported that childhood BT survivors show decreased employment, less education beyond high school, and less independent living (Ness et al., 2010). Much has been written about BT treatment, survival, and medical outcome; however, few researchers have addressed the functional outcome of patients with brain tumour from a rehabilitation perspective. Indeed, the impact of late effects on function and daily living activities are poorly documented and quantified; existing research that measured performance in activities of daily living (ADL), from an objective perspective using standardized evaluation tools, are rare in the literature (Parks et al., 2009).

The lack of detailed information regarding the functional outcome of survivors can result from many factors, including the use of socio-demographic indicators to represent function (i.e. insurability), self-report questionnaires or instruments based on broad functional classifications. Hence, a good description of how the large array of late effects affect the BT survivors' performance in ADL is not yet available. As the survivors are

entering a state in their life where they are expected to be independent, find a job, and to pursue higher education, the literature does not inform us on how they are struggling with their everyday living. This information is important for occupational therapists working in paediatric oncology who play an important role in assisting with children's participation in their life occupations. Occupational therapists can assess for difficulties in the areas of daily living and provide interventions to enable both children's occupational participation and well-being.

With increasing life expectancy in cancer patients, there has been a move toward assessment of quality of life to supplement medical measures in evaluating the adverse effects of cancer on the lives of survivors (Eiser & Berrenberg, 1995). Health-related quality of life (HRQoL) is a multidimensional construct used to assess the impact of a disease and its treatment in terms of physical, social, emotional, cognitive, and overall well-being (Berra et al., 2007; WHO, 1996). HRQoL is best evaluated with self-reported instruments, as the person is the ultimate judge of his or her own health and treatment outcome. Among childhood cancer survivors, it has been proven that BT survivors have among the lowest HRQoL secondary to a complex array of treatment-related late effects (McDougall & Tsonis, 2009; Zeltzer et al., 2009). Associations among physical performance, executive function, and HRQoL outcomes among adult survivors of childhood cancer have been studied before (Ness et al., 2008), but not specifically with the BT survivor population. Occupational therapy advocates for the use of quality of life in practice, research, and as an outcome measure, believing engagement in valued occupations allows people to express their identity and gives worth and meaning to people's

lives (Liddle, 2000).

The present study addresses the performance in ADL of adolescent and young adult survivors of childhood BT and its association with HRQoL, as they reflect the everyday life of survivors beyond the acute diagnosis and treatment phases. The specific aims were: (1) to estimate the extent to which young adult survivors of childhood BT achieve a level of performance in ADL that is comparable to their peers; and (2) to assess the association between observed limitations in motor and process skills and the HRQoL of BT survivors.

5.3 METHODS

Participants

A cross-sectional study was conducted with a convenience sample of brain tumour survivors recruited from a long-term follow-up clinic at CHU Ste-Justine in Montreal. The CHU Sainte-Justine is a leader in haematology-oncology care and research in North America and enjoys an international reputation. It serves 60% of the paediatric population of Quebec and is treating close to 1,100 children with cancer each year, including 40-50 new brain tumours per year. Brain tumour survivors were recruited from the haematology-oncology department follow-up clinic. Some patients were also recruited from a list of patients who had been transferred to an adult hospital center. To be included, the participants met the following criteria: (a) treated between 1987 and 2007 inclusively at CHU Ste-Justine and aged ≤ 21 years during that period, (b) age ≥ 16 years at the time of the study, (c) brain tumour as the first cancer occurrence, (d) being at least 3 years off treatment with no recurrence or

progression and at least 5 years since diagnosis. Excluded from participation were persons who: (a) had a tumour located in the spinal cord, (b) were treated by surgery only, (c) had a pre-existing comorbid conditions not related to the cancer or treatments that might have affected their functional outcome.

Sample size calculations were based on the main outcome measure (AMPS). For the age group 16-29, the standard deviations are 0.52 for motor skills and 0.43 for process skills. For the effect size, according to the literature, a change of at least 0.3 logit for motor or process ability measures indicates a significant change (Magalhaes et al., 1996; Silverstein et al., 1992). Based on a level of significance of α (1-sided) = 0.05, β = 0.20 and SES of 0.9, sample sizes of 36 and 26 respectively for motor and process skills was required, therefore 36 participants were recruited.

The study protocol was approved by the Research Ethics Board of CHU Ste-Justine. Written informed consent was obtained from participants ≥ 18 years old and from parents for participants < 18 years old.

Data collection

Every month a list of the BT survivors attending their annual appointment at the long term follow up clinic at CHU Ste-Justine was provided by the research nurse. The list of transferred patients was also consulted on a regular basis. The main researcher approached patients who met the eligibility criteria by telephone. Patients who agreed to participate were asked to give their written, informed consent. The medical charts were

then reviewed and clinical data were abstracted to obtain relevant material on the medical condition, treatment information, and past history. It also ensured that the participant met all the inclusion/exclusion criteria. An appointment for the assessment was scheduled during their follow-up visit at Ste-Justine or at a time of their convenience. For the participants living in the Montreal area, the possibility of conducting the assessment at home was also proposed for the patient's convenience. During the appointment, the participants were first asked to fill out the HRQoL questionnaire as well as a socio-demographic questionnaire. Afterwards, the functional assessment was administered to study participants by the main researcher. The evaluation took in average 1 to 2 hours to complete, and all subjects were assessed over a period of 10 months.

Measures

A standardized objective measure, the Assessment of Motor and Process Skills (AMPS) (Fisher, 2010), was used to evaluate the quality of activity of daily living (ADL) task performance. The AMPS evaluates 16 motor and 20 process skills, that are the smallest observable units of ADL task performance, using a four-point ordinal scale, ranging from deficient = 1 to competent = 4, according to very explicit, specific criteria. The AMPS skills are goal-directed actions and the quality of each skill is evaluated within the context of the person performing daily life tasks. ADL motor skills are observable actions used to move oneself and task objects (e.g. "reaches", "bends" and "calibrates"). ADL process skills are observable actions used to organize and adapt task actions to prevent or overcome problems (e.g. "initiates", "chooses" and "organizes"). Physical abilities and cognition are related to some aspects of the ADL motor and process skills, however, the

AMPS assessment is not designed to test physical or cognitive impairments, it is used to measure observable goal-directed skills related to enacting an ADL task performance. Over 120 separate ADL tasks are standardized for use with the AMPS. During AMPS administration, an occupational therapist observes a patient performing two culturally relevant ADL tasks with which he/she has familiarity and prior experience from the list of calibrated AMPS tasks. The occupational therapist rates quality of performance on each of the 16 ADL motor and 20 ADL process skills using the four-point ordinal scale. The AMPS has been standardized on over 125,000 clients worldwide. Studies support the reliability and validity of the AMPS across age groups and gender (Hayase et al., 2004; Merritt & Fisher, 2003) and its sensitivity as an outcome measure (Cooke et al., 2000; Graff et al., 2006; Kottorp, Bernspang, & Fisher, 2003). Even more than the direct demonstration of abilities, the AMPS process scale provides further information regarding the extent to which the person has overcome residual neuromuscular, biomechanical, cognitive, and psychosocial impairments and capacity limitations by using alternative or compensatory strategies during task performance (Fisher, 2010). The AMPS has been used in a study evaluating the ADL performance of pediatric sarcoma survivors (Parks et al., 2009) and it allowed the research team to collect new and highly relevant information on this population. The evaluator was previously trained in the use of the evaluation tool and calibrated with demonstrated rater reliability, per standardized procedure.

HRQoL was evaluated by having participant complete the Medical Outcome Survey 12-Item Short-Form Health Survey (SF-12). The SF-12 is

a generic health profile that produces two overall summary scores, the Physical Component Summary (PCS) and the Mental Component Summary (MCS). The PCS is primarily based on the original Medical Outcomes Survey 36-item Short Form (SF-36) domains of physical functioning, role limitations due to physical health problems, bodily pain and general health perception, while the MCS is primarily based on the domains of vitality, social functioning, role limitation due to emotional problems and mental health (Ware & Sherbourne, 1992). The PCS and MCS are standardized to a mean of 50, with scores above and below 50 representing better than and poorer than average summaries, respectively (Ware et al., 1996; Ware & Sherbourne, 1992) and a 2 to 3 point difference is considered clinically meaningful (Ware et al., 1996). The SF-12 is widely used with numerous health conditions and has been previously used with the childhood cancer survivors' population (Bober et al., 2013; O'Leary, Diller, & Recklitis, 2007). The SF-12 questionnaire was used instead of the SF-36 because it is shorter and it is therefore more appropriate with individuals with learning disabilities and cognitive impairments such as short attention span.

Data Analysis

Descriptive statistics (mean, SD, %) were calculated for the socio-demographic and clinical characteristics of the eligible participants.

AMPS computer-scoring software was used to generate ADL motor and ADL process ability measures for each study participant. This program uses many-faceted Rasch analysis to convert the raw, ordinal ADL motor

and ADL process skills scores to linear ADL motor and ADL process ability measures expressed in equal-interval, log odds probability units, termed “logits”. Mean and 95% confidence intervals (CI) for ADL motor and ADL process ability measures were calculated. Differences in mean ADL motor and ADL process ability with the norms were determined using a one-sample t-test ($p < 0.05$).

Raw scores from the SF-12 were converted to T scores (range 0 – 100) and differences in mean MCS and PCS scores with the norms were determined using a one-sample t-test ($p < 0.05$).

Multiple linear regression was used to evaluate the relationship between ADL motor and ADL process ability measures versus HRQoL for each subscale (MCS and PCS). Simple linear regressions were first performed to evaluate the association between each subscale of the SF-12 with each of the ADL performance skills. Then, the potential for confounding for age, gender, time since treatment, age at diagnosis, tumour type and location, treatment type, dose of radiation and chronic health condition were tested using simple linear regression. Each potential confounding variable was assessed for its relationship with the outcome (HRQoL) and with each of the predictor variables (motor and process skills). Those variables found to have a significant effect on both the outcome and one of the explanatory variables were added to the model. Statistical significance was set at the 5% level. Data analyses were performed using SPSS version 20.

5.4 RESULTS

Characteristics of the study population

To recruit 36 participants, 42 persons were contacted, resulting in a 86% participation rate. Reasons for refusal to participate included no time (2) and no interest in the study (4). The socio-demographic and clinical characteristics of the participants are shown in Table 1. The participants in our study differed from the statistics available from Health Canada (1996). (1996). Indeed, in Canada, the incidence of brain tumour is approximately 20% higher in boys compared to girls when only 39% of our participants are boys. As for the diagnosis, half of the tumour type in this age group typically are astrocytomas or gliomas, and 20% are medulloblastomas, although in our study they account for 11% and 44% respectively.

Activities of daily living

Means and 95% CI for ADL motor and ADL process ability measures for the survivors are shown in Table 2. Both the ADL motor ability and the ADL process were significantly lower for the survivors compared to the 16-29 age group norms ($p < 0.05$).

Health-related Quality of life and its association with Activities of daily living

The results for the health related quality of life as evaluated by the SF-12 are shown in Table 3. Both the mental and physical summary scales are in the average of the general population with means of 50,27 and 48,16 respectively. In addition, only 4 participants (11%) had a result below the norms for the mental summary scale and 6 (17%) for the physical summary scale.

The associations between each ADL performance skill (motor and process) and each HRQoL summary scale are shown in Figures 1-4. For the multiple linear regression models, after adjusting for gender and chronic health conditions, the level of performance in ADL skills (motor and process) were significantly associated with overall physical health ($r^2=0.5$) and after adjusting for time since treatment and chronic health conditions with mental health ($r^2=0.3$).

5.5 DISCUSSION

The purpose of this study was to examine the ADL functioning among young adults' survivors of childhood BT as well as their HRQoL. To our knowledge, this study is one of the first to document specific deficits in ADLs using an objective, well-standardized performance-based measure. The study showed that the ADL functioning of BT survivors was significantly lower than that of the age norms but that they have a HRQoL similar to the general population. Furthermore, this study showed that functional outcome is positively associated with self-reported physical and mental health.

As young survivors reach adulthood, they are facing new challenges. Young adults are now expected to live independently and to contribute to their society by working. However, the combination of motor and process skills' deficits can make them unable to be as productive as what employers might expect and to lead a "normal life" according to our society standards. For example, in our study, only few participants live in an apartment independently and, of the participants who have finished

school, only about half have a full time job. These basic aspects of a life are not commonly addressed in our health system that focuses more on medical outcomes. Especially if the survivors consider they have a satisfying HRQoL, they might underreport their difficulties when meeting with their medical team. Over the past 2 decades, the cancer literature has reported variable results regarding functional abilities of long-term BT survivors (Aarsen et al., 2006; Armstrong et al., 2009; Bhat et al., 2005; Boman et al., 2009; Fouladi et al., 2005). The selection of functional assessment tools for cancer patients has been particularly problematic, especially since many questionnaire completed by cancer patients were not designed specifically to elicit information about function. Because a performance-based and standardized assessment was used in this study, it was able to give more accurate, real-life information on the functional status of survivors. The findings from this study highlight the fact that the late effects experienced by the survivors affect not only their socio-demographic outcomes, but also their basic day-to-day life and activities, such as cooking and cleaning, as well as their capacity to live independently.

Our findings are consistent with those of another study (Parks et al., 2009), which reported that treatment late effects on performance of daily living activities are more widespread than reported in the current literature in the paediatric sarcoma survivors' population. The present study also suggests that the functional impact of BT is underreported in the literature.

In the AMPS assessment, there is a very strong interaction between the underlying physical and cognitive impairments and the AMPS motor and

process skills scale (Fisher, 2010). Deficits in any of the systems (musculoskeletal, neurologic, cognitive) can result in either ADL motor or process skill deficits. For example, when problems occur in motor skills, there is an increased demand on the ADL process skills that reflect the underlying organizational and adaptive capacities of the individual. The other way is equally true, when problems occur in process skill, the individual may have a decreased capacity to adapt to or compensate for ADL motor skill deficits and may be at even greater risk for losing independence. The strong interaction between the two scales can explain that the strength of the relationship with HRQoL is similar for motor and process skills. Furthermore, the results for both motor and process skills document justification as to the participants' need for rehabilitation services to optimize their performance in ADLs.

As for the HRQoL, the findings of this study are surprising. Overall, the results indicate that survivors report good HRQoL. These findings are consistent with another study, concluding that the BT survivors did not differ from the population norms for the majority of the HRQoL domains (Aukema et al., 2013). The fact that they report good HRQoL in comparison with population norms could be explained by the "response shift" phenomenon. That is, experiencing childhood cancer inoculates individuals to other negative life experiences and provides them with feelings of life satisfaction and overall psychological well-being (Zeltzer et al., 2008).

Understanding the association between performance limitations and HRQoL is important for rehabilitation professionals as rehabilitative

intervention designed to address activity limitations may eventually improve HRQoL. It provides an avenue for optimal role attainment among those childhood cancers survivors whose disability interferes with performance. Similar to the results of another study with a cohort of childhood cancer survivors (Ness et al., 2008), participants with performance limitation were associated with reports of poorer HRQoL. However, the relatively weak relationship between ADL performance and HRQoL suggests that other factors have to be taken into consideration to explain the survivors' perceived health. For example, factors such as social support and satisfaction with physical appearance are some of the common challenges identified by young cancer survivors (D'Agostino & Edelstein, 2013) that were not addressed in this study. Also, we may conclude that survivors might not benefit from services because they tend to inflate their functional status. It is therefore important to ask a relative about their needs or to assess them extensively in order to make sure survivors have access to the appropriate medical, rehabilitation, or community services.

Limitations and future research

We acknowledge that our study has potential limitations. The cross-sectional nature of this study only provides a snapshot of the situation and the impact of late effects over time is therefore unknown in this sample. Moreover, the small number of subjects in this study did not allow us to perform additional analyses between subgroups. Other limitations are the absence of proper control group and the restriction of the data to one hospital that may limit the generalizability of the results. The HRQoL outcome compared to a control group instead of the general populations

norms would have allowed us to evaluate the extent to which the outcome is significantly different from a group of young adults without an history of cancer.

Rehabilitation programs to optimize both function and quality of life should be developed for adult survivors as well as for children currently undergoing therapy. A knowledge translation strategy should also be planned to ensure clinicians working in the area of childhood cancer are informed of these potential vulnerabilities enable them to help as much as possible their patients and their families. The findings also provide a rationale for larger, multi-center studies.

Conclusion

Our study is one of the first to document specific deficits in ADLs using an objective, well-standardized performance-based measure. Our results from this study underline the significance of the impact of childhood BT and related treatments on the functional outcome of survivors. On average, adult survivors of childhood BT have significantly lower motor and process skills than the age norms but good HRQoL. Furthermore, this research shows the positive association between performance in ADL, from an objective perspective, and HRQoL from the participant's perspective.

IMPLICATIONS FOR OCCUPATIONAL THERAPY PRACTICE

- Increase awareness of the potential for functional limitations in survivors of BT and importance of referral to rehabilitation professionals;
- Guide the therapists in predicting the functional outcome and determining priorities for intervention and follow-up;
- Highlight the importance for professionals to provide comprehensive education to patients about their own potential vulnerabilities.

ACKNOWLEDGMENT

This research was supported by the Coast-to-Coast Foundation. We would like to acknowledge the contribution of the oncology rehabilitation team of the CHU Ste-Justine and to thank the participants for their very precious time and generosity.

TABLES AND FIGURES

Table 5.1 Personal and Clinical Characteristics of the Study Participants
mean (SD) or N(%) (n=36)

Characteristics	
Age at evaluation (16-29 years)	21,0 ± 3,3
Gender	22 female : 14 male
Level of education (highest diploma)	
Elementary school	13 (36,1)
High school	9 (25,0)
Cegep or professional school	11 (30,6)
University	3 (8,4)
Occupation	
Studying or working full-time	20 (55,6)
Studying special program, sheltered employment or part-time	13 (36,1)
Unemployed	3 (8,3)
Independence status	
Independent	6 (16,7)
Living with family or in resource	30 (83,3)
Time since end of treatment (years)	10,1 ± 3,8
Age at diagnosis (years)	8,9 ± 5,1
Tumour type	
Medulloblastoma or PNET	23 (63,9)
Astrocytoma or glioma	5 (13,9)
Other	8 (22,2)
Tumour location	
Posterior fossa	19 (52,8)
Supratentorial or parasellar	17 (47,2)
Type of treatment	
No radiation	1 (2,8)
Cranial radiation	7 (19,4)
Cranial and spinal radiation	28 (77,8)
Radiation dose	
<55Gy	16 (44,5)
≥55Gy	18 (55,5)
Chronic health conditions	
Endocrine	30 (83,3)
Musculoskeletal	17 (47,2)
Neurologic or neurosensory	27 (75,0)
Rehabilitation Services	
Occupational Therapy	24 (66,7)
Physiotherapy	27 (75,0)
Psychology or neuropsychology	24 (66,7)
Speech Therapy	4 (11,1)

Table 5.2 Results of AMPS Evaluation (ADL Motor and Process Ability) in comparison with age norms (Mean +/- SD, p-value) (n=36)

	Survivors	Norms	p
Motor skills (logits)			<0.001
Mean	1,77	2,95	
SD	0,77	0,53	
Min - Max	-0,04 – 3,06		
Process skills (logits)			<0.001
Mean			
SD	1,29	2,01	
Min - Max	0,64 -0,43 – 2,59	0,43	

Table 5.3 Results of SF-12 questionnaire in comparison with population norms. (Mean +/- SD, p-value) (n=36)

	Survivors	Norms	p
Mental Component Scale			0,465
Mean	50,27	50	
SD	7,55	10	
Min - Max	37,89 – 63,01		
Physical Component Scale			0,106
Mean	48,16	50	
SD	9,33	10	
Min - Max	25,36 – 60,45		

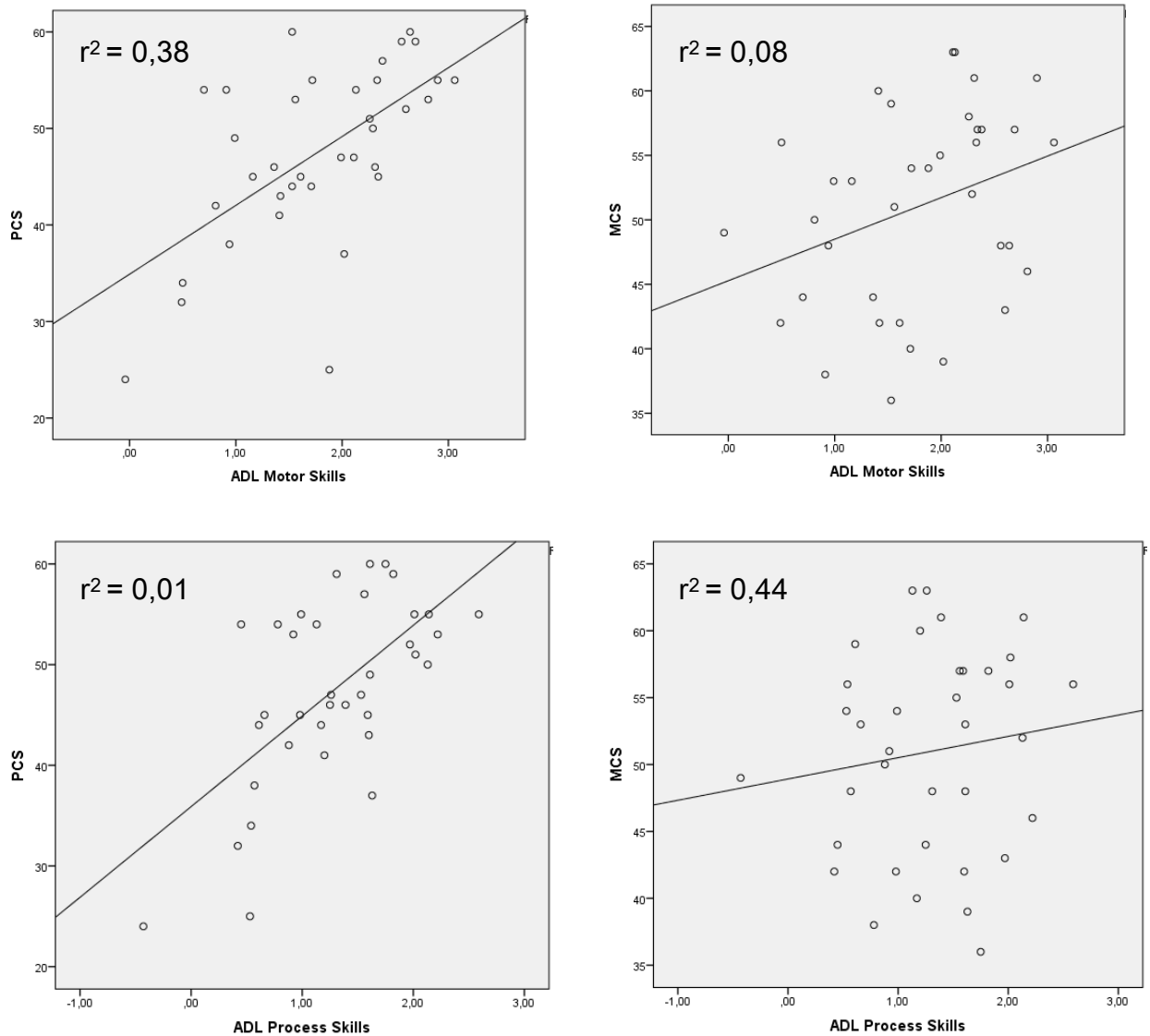


Figure 5.1 These charts illustrate association between motor skills, process skills and scores on the Mental Component Scale (MCS) and Physical Component Scale (PCS) scales of the SF-12. Higher scores on motor and process skills represent high performance. Higher scores on MCS and PCS scales represent good Health related Quality of Life.

LIST OF REFERENCES

- Aarsen, F. K., Paquier, P. F., Reddingius, R. E., Streng, I. C., Arts, W. F., Evera-Preesman, M., & Catsman-Berrevoets, C. E. (2006). Functional outcome after low-grade astrocytoma treatment in childhood. *Cancer*, *106*(2), 396-402. doi: 10.1002/cncr.21612
- Armstrong, G. T., Liu, Q., Yasui, Y., Huang, S., Ness, K. K., Leisenring, W., Packer, R. J. (2009). Long-term outcomes among adult survivors of childhood central nervous system malignancies in the Childhood Cancer Survivor Study. *J Natl Cancer Inst*, *101*(13), 946-958. doi: 10.1093/jnci/djp148.
- Aukema, E. J., Netteke Schouten-van Meeteren, A. Y., Last, B. F., Maurice-Stam, H., & Grootenhuis, M. A. (2013). Childhood Brain Tumor Survivors at Risk for Impaired Health-related Quality of Life. *J Pediatr Hematol Oncol* *35*(8).
- Berra, S., Ravens-Sieberer, U., Erhart, M., Tebe, C., Bisegger, C., Duer, W., Rajmil, L. (2007). Methods and representativeness of a European survey in children and adolescents: the KIDSCREEN study. *BMC Public Health*, *7*, 182. doi: 10.1186/1471-2458-7-182
- Bhat, S. R., Goodwin, T. L., Burwinkle, T. M., Lansdale, M. F., Dahl, G. V., Huhn, S. L., et al. (2005). Profile of daily life in children with brain tumors: an assessment of health-related quality of life. *J Clin Oncol*, *23*(24), 5493-5500. doi: 10.1200/JCO.2005.10.190
- Bober, S. L., Zhou, E. S., Chen, B., Manley, P. E., Kenney, L. B., & Recklitis, C. J. (2013). Sexual function in childhood cancer survivors: a report from Project REACH. *J Sex Med*, *10*(8), 2084-2093. doi: 10.1111/jsm.12193
- Boman, K. K., Hoven, E., Anclair, M., Lannering, B., & Gustafsson, G. (2009). Health and persistent functional late effects in adult survivors of childhood CNS tumours: a population-based cohort study. *Eur J Cancer*, *45*(14), 2552-2561. doi: 10.1016/j.ejca.2009.06.008
- Canadian Cancer Society (2011). *Canadian Cancer Statistics 2011*. Toronto, ON: Canadian Cancer Society's Advisory Committee on Cancer Statistics.
- Cooke KZ, F. A., Mayberry W, Fisher A.G., et al. . (2000). Differences in activities of daily living process skills of persons with and without Alzheimer's disease. *Occup Ther J Res*, *20*, 87-103.

- D'Agostino, N. M., & Edelstein, K. (2013). Psychosocial challenges and resource needs of young adult cancer survivors: implications for program development. *J Psychosoc Oncol*, 31(6), 585-600. doi: 10.1080/07347332.2013.835018
- Eiser, C., & Berrenberg, J. L. (1995). Assessing the impact of chronic disease on the relationship between parents and their adolescents. *J Psychosom Res*, 39(2), 109-114.
- Fisher, A. G. (2006). *Assessment of motor and process skills, Vol. 1: Development, standardization, and administration manual*, 6th ed. Ft. Collins, CO: Three Star Press.
- Fouladi, M., Gilger, E., Kocak, M., Wallace, D., Buchanan, G., Reeves, C., Mulhern, R. (2005). Intellectual and functional outcome of children 3 years old or younger who have CNS malignancies. *J Clin Oncol*, 23(28), 7152-7160. doi: 10.1200/JCO.2005.01.214
- Geenen, M. M., Cardous-Ubbink, M. C., Kremer, L. C., van den Bos, C., van der Pal, H. J., Heinen, R. C., Van Leeuwen, F. E. (2007). Medical assessment of adverse health outcomes in long-term survivors of childhood cancer. *JAMA*, 297(24), 2705-2715. doi: 10.1001/jama.297.24.2705
- Graff, M. J., Vernooij-Dassen, M. J., Thijssen, M., Dekker, J., Hoefnagels, W. H., & Rikkert, M. G. (2006). Community based occupational therapy for patients with dementia and their care givers: randomised controlled trial. *BMJ*, 333(7580), 1196. doi: 10.1136/bmj.39001.688843.BE
- Hayase D, M. D., Thimmaiah D, et al. . (2004). Age-related changes in activities of daily living ability. *Aust Occup Ther J*, 51, 192-198.
- Health Canada (1996). *Statistics Canada*. Government of Canada.
- Jemal, A., Murray, T., Samuels, A., Ghafoor, A., Ward, E., & Thun, M. J. (2003). Cancer statistics, 2003. *CA Cancer J Clin*, 53(1), 5-26.
- Kottorp, A., Bernspang, B., & Fisher, A. G. (2003). Validity of a performance assessment of activities of daily living for people with developmental disabilities. *J Intellect Disabil Res*, 47(Pt 8), 597-605.
- Liddle J, M. K. (2000). Quality of life: an overview of issues for use in occupational therapy outcome measurement. *Aus Occup Ther J*, 47, 77-85.
- Macedoni-Luksic, M., Jereb, B., & Todorovski, L. (2003). Long-term sequelae in children treated for brain tumors: impairments, disability, and handicap. *Pediatr Hematol Oncol*, 20(2), 89-101.

- Magalhaes, T., Hamonet, C., de Sousa, M. J., Matos, E., & da Costa, J. P. (1996). Occupational handicap in victims of limb injuries. *Med Law*, 15(1), 135-141.
- McDougall, J., & Tsonis, M. (2009). Quality of life in survivors of childhood cancer: a systematic review of the literature (2001-2008). *Support Care Cancer*, 17(10), 1231-1246. doi: 10.1007/s00520-009-0660-0
- Merritt, B. K., & Fisher, A. G. (2003). Gender differences in the performance of activities of daily living. *Arch Phys Med Rehabil*, 84(12), 1872-1877.
- National Research Council (2005). From Cancer Patient to Cancer Survivor: Lost in Transition. In T. N. A. Press (Ed.). Washington, DC.
- Ness, K. K., Gurney, J. G., Zeltzer, L. K., Leisenring, W., Mulrooney, D. A., Nathan, P. C., Mertens, A. C. (2008). The impact of limitations in physical, executive, and emotional function on health-related quality of life among adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. *Arch Phys Med Rehabil*, 89(1), 128-136.
- Ness, K. K., Morris, E. B., Nolan, V. G., Howell, C. R., Gilchrist, L. S., Stovall, M., et al. (2010). Physical performance limitations among adult survivors of childhood brain tumors. *Cancer*, 116(12), 3034-3044.
- O'Leary, T. E., Diller, L., & Recklitis, C. J. (2007). The effects of response bias on self-reported quality of life among childhood cancer survivors. *Qual Life Res*, 16(7), 1211-1220. doi: 10.1007/s11136-007-9231-3
- Parks, R., Rasch, E. K., Mansky, P. J., & Oakley, F. (2009). Differences in activities of daily living performance between long-term pediatric sarcoma survivors and a matched comparison group on standardized testing. *Pediatr Blood Cancer*, 53(4), 622-628. doi: 10.1002/pbc.22101
- Silverstein, B., Fisher, W. P., Kilgore, K. M., Harley, J. P., & Harvey, R. F. (1992). Applying psychometric criteria to functional assessment in medical rehabilitation: II. Defining interval measures. *Arch Phys Med Rehabil*, 73(6), 507-518.
- Ware, J., Jr., Kosinski, M., & Keller, S. D. (1996). A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care*, 34(3), 220-233.

- Ware, J. E., Jr., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*, 30(6), 473-483.
- World Health Organization. (1996). Introduction, Administration, Scoring and Generic Version of the Assessment *WHOQOL-BREF*. Geneva: World Health Organization.
- Zeltzer, L. K., Lu, Q., Leisenring, W., Tsao, J. C., Recklitis, C., Armstrong, G., Ness, K. K. (2008). Psychosocial outcomes and health-related quality of life in adult childhood cancer survivors: a report from the childhood cancer survivor study. *Cancer Epidemiol Biomarkers Prev*, 17(2), 435-446.
- Zeltzer, L. K., Recklitis, C., Buchbinder, D., Zebrack, B., Casillas, J., Tsao, J. C., et al. (2009). Psychological status in childhood cancer survivors: a report from the Childhood Cancer Survivor Study. *J Clin Oncol*, 27(14), 2396-2404.

CHAPTER 6: CONCLUSION AND SUMMARY

From the day of the diagnosis, childhood brain tumour is a rare and very serious condition that impacts significantly on all aspects of the child and its family's lives. In order to help them manage their everyday life after the completion of the treatment, it is important to understand how the late effects affect their performance in activities of daily living (ADL), from an objective perspective, while considering their perspective on their own health status. Furthermore, it is important to identify which variables are likely to be associated with a low level of performance in order to target the more vulnerable populations. This thesis has addressed these objectives in the population under study. From our findings we are able to draw several important conclusions on the functional impact, the health related quality of life, as well as what are the most important variables that are associated with the level of performance in ADL.

In the first manuscript, we determined which factors for specific impairments are likely to be associated with performance limitations. Identifying these variables has important clinical implications, as it can provide information on which subgroups of patients could benefit greatly from rehabilitation services on a long-term basis.

In the second manuscript, we estimated the extent to which young adult survivors of childhood brain tumour achieve a level of performance in activities of daily living that is comparable to their peers. In addition, we assessed the association between observed limitations in motor and

process skills and health related quality of life. These findings have important implications for clinical practice, as it emphasizes the strong need for rehabilitation services and can provide target or directions for intervention.

While there remains ongoing work to do in this relatively new area of research, the field has advanced to a point of also directing resources toward the development of rehabilitation interventional studies. A thorough understanding of the multiple domains affected by childhood brain tumour survivors and the interconnectedness of their late effects is necessary to undertake such studies. Furthermore, it will be important to ensure the translation of research findings into clinical practice for the benefit of the survivors in order to support them in the achievement of the best possible outcome at long term.

REFERENCES

1. Smith, M.A. and L.A.G. Ries, *Childhood Cancer: Incidence, Survival, and Mortality*, in *Principles and Practice of Pediatric Oncology*, P.D. Pizzo PA, Eds., Editor 2002, Lippincott Williams & Wilkins: Philadelphia.
2. Canadian Cancer Society, *Statistiques canadiennes sur le cancer*, 2011. p. 63-79.
3. Mariotto, A. B., Rowland, J. H., Yabroff, K. R., Scoppa, S., Hachey, M., Ries, L., & Feuer, E. J. (2009). Long-term survivors of childhood cancers in the United States. *Cancer Epidemiol Biomarkers Prev*, 18(4), 1033-1040.
4. Leigh, S.A., *Defining our destiny*, in *A Cancer Survivor's Almanac: Charting the Journey*, e. Hoffman B, Editor 1996, Chronimed Publishing: Minneapolis, MN. p. 261-271.
5. National Coalition for Cancer Survivorship, *A National Action Plan for Cancer Survivorship: Advancing Public Health Strategies*, 2004.
6. National Research Council, *From Cancer Patient to Cancer Survivor: Lost in Transition*, T.N.A. Press, Editor 2005: Washington, DC.
7. Robinson, K. E., Kuttesch, J. F., Champion, J. E., Andreotti, C. F., Hipp, D. W., Bettis, A., Barnwell, A., Compas, B. E. (2010). A quantitative meta-analysis of neurocognitive sequelae in survivors of pediatric brain tumors. *Pediatr Blood Cancer*, 55(3), 525-531.
8. American Cancer Society, *Cancer Facts & Figure 2009*, 2009, American Cancer Society: Atlanta, GA.
9. Canadian Cancer Society., *Canadian Cancer Statistics 2008*, 2008.
10. Memorial Sloan Kettering Cancer Center. *Brain tumors*. 2014 retrieved on 03/26/2014; Available from: <http://www.mskcc.org/pediatrics/childhood/pediatric-brain-tumors>
11. Lanzkowsky, P., *Central Nervous System Malignancies*, 2011, San Dieg: Academic Press.
12. Turner, C.D., Rey-Casserly, C., Liptak, C. C., & Chordas, C., *Late effects of therapy for pediatric brain tumor survivors*. J Child Neurol, 2009. 24(11): p. 1455-63.
13. Jemal, A., Murray, T., Samuels, A., Ghafoor, A., Ward, E., & Thun, M. J., *Cancer statistics, 2003*. CA Cancer J Clin, 2003. 53(1): p. 5-26.

14. Hocking, M.C., Hobbie, W. L., Deatrick, J. A., Lucas, M. S., Szabo, M. M., Volpe, E. M., & Barakat, L. P., *Neurocognitive and family functioning and quality of life among young adult survivors of childhood brain tumors*. Clin Neuropsychol, 2011. **25**(6): p. 942-62.
15. Boman, K.K., Hoven, E., Anclair, M., Lannering, B., & Gustafsson, G., *Health and persistent functional late effects in adult survivors of childhood CNS tumours: a population-based cohort study*. Eur J Cancer, 2009. **45**(14): p. 2552-61.
16. Oeffinger, K.C., Mertens, A. C., Sklar, C. A., Kawashima, T., Hudson, M. M., Meadows, A. T., . Friedman, D. L., Marina, N., Hobbie, W., Kadan-Lottick, N. S., Schwartz, C. L., Leisenring, W., Robison, L. L., *Chronic health conditions in adult survivors of childhood cancer*. N Engl J Med, 2006. **355**(15): p. 1572-82.
17. Geenen, M.M., Cardous-Ubbink, M. C., Kremer, L. C., van den Bos, C., van der Pal, H. J., Heinen, R. C., et al., *Medical assessment of adverse health outcomes in long-term survivors of childhood cancer*. JAMA, 2007. **297**(24): p. 2705-15.
18. Oeffinger, K.C., P.C. Nathan, and L.C. Kremer, *Challenges after curative treatment for childhood cancer and long-term follow up of survivors*. Hematol Oncol Clin North Am, 2010. **24**(1): p. 129-49.
19. Armstrong, G.T., *Long-term survivors of childhood central nervous system malignancies: the experience of the Childhood Cancer Survivor Study*. Eur J Paediatr Neurol, 2010. **14**(4): p. 298-303.
20. Anderson, D.M., Rennie, K. M., Ziegler, R. S., Neglia, J. P., Robison, L. R., & Gurney, J. G., *Medical and neurocognitive late effects among survivors of childhood central nervous system tumors*. Cancer, 2001. **92**(10): p. 2709-19.
21. Bowers, D.C., Liu, Y., Leisenring, W., McNeil, E., Stovall, M., Gurney, J. G., et al., *Late-occurring stroke among long-term survivors of childhood leukemia and brain tumors: a report from the Childhood Cancer Survivor Study*. J Clin Oncol, 2006. **24**(33): p. 5277-82.
22. Gurney, J.G., Kadan-Lottick, N. S., Packer, R. J., Neglia, J. P., Sklar, C. A., Punyko, J. A., et al., *Endocrine and cardiovascular late effects among adult survivors of childhood brain tumors: Childhood Cancer Survivor Study*. Cancer, 2003. **97**(3): p. 663-73.
23. Mulhern, R.K., Merchant, T. E., Gajjar, A., Reddick, W. E., & Kun, L. E., *Late neurocognitive sequelae in survivors of brain tumours in childhood*. Lancet Oncol, 2004. **5**(7): p. 399-408.

24. Packer, R.J., Gurney, J. G., Punyko, J. A., Donaldson, S. S., Inskip, P. D., Stovall, M., et al., *Long-term neurologic and neurosensory sequelae in adult survivors of a childhood brain tumor: childhood cancer survivor study*. J Clin Oncol, 2003. **21**(17): p. 3255-61.
25. Ness, K.K., Morris, E. B., Nolan, V. G., Howell, C. R., Gilchrist, L. S., Stovall, M., et al., *Physical performance limitations among adult survivors of childhood brain tumors*. Cancer, 2010. **116**(12): p. 3034-44.
26. Armstrong, G.T., Liu, Q., Yasui, Y., Huang, S., Ness, K. K., Leisenring, W., et al., *Long-term outcomes among adult survivors of childhood central nervous system malignancies in the Childhood Cancer Survivor Study*. J Natl Cancer Inst, 2009. **101**(13): p. 946-58.
27. Kunin-Batson, A., Kadan-Lottick, N., Zhu, L., Cox, C., Bordes-Edgar, V., Srivastava, D. K., et al., *Predictors of independent living status in adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study*. Pediatr Blood Cancer, 2011. **57**(7): p. 1197-203.
28. Ullrich, N.J., Robertson, R., Kinnamon, D. D., Scott, R. M., Kieran, M. W., Turner, C. D., et al., *Moyamoya following cranial irradiation for primary brain tumors in children*. Neurology, 2007. **68**(12): p. 932-8.
29. Coradini, P.P., Cigana, L., Selistre, S. G., Rosito, L. S., & Brunetto, A. L., *Ototoxicity from cisplatin therapy in childhood cancer*. J Pediatr Hematol Oncol, 2007. **29**(6): p. 355-60.
30. Gayre, G.S., Scott, I. U., Feuer, W., Saunders, T. G., & Siatkowski, R. M., *Long-term visual outcome in patients with anterior visual pathway gliomas*. J Neuroophthalmol, 2001. **21**(1): p. 1-7.
31. Johannesen, T.B., Rasmussen, K., Winther, F. O., Halvorsen, U., & Lote, K., *Late radiation effects on hearing, vestibular function, and taste in brain tumor patients*. Int J Radiat Oncol Biol Phys, 2002. **53**(1): p. 86-90.
32. Neglia, J.P., Friedman, D. L., Yasui, Y., Mertens, A. C., Hammond, S., Stovall, M., et al., *New primary neoplasms of the central nervous system in survivors of childhood cancer: a report from the Childhood Cancer Survivor Study*. J Natl Cancer Inst, 2006. **98**(21): p. 1528-37.
33. Henderson, T.O., Whitton, J., Stovall, M., Mertens, A. C., Mitby, P., Friedman, D., et al., *Secondary sarcomas in childhood cancer*

- survivors: a report from the Childhood Cancer Survivor Study.* J Natl Cancer Inst, 2007. **99**(4): p. 300-8.
34. Perkins, J.L., Liu, Y., Mitby, P. A., Neglia, J. P., Hammond, S., Stovall, M., et al., *Nonmelanoma skin cancer in survivors of childhood and adolescent cancer: a report from the childhood cancer survivor study.* J Clin Oncol, 2005. **23**(16): p. 3733-41.
 35. Edelstein, K., Spiegler, B. J., Fung, S., Panzarella, T., Mabbott, D. J., Jewitt, N., et al., *Early aging in adult survivors of childhood medulloblastoma: long-term neurocognitive, functional, and physical outcomes.* Neuro Oncol, 2011. **13**(5): p. 536-45.
 36. Gragert, M.N. and M.D. Ris, *Neuropsychological late effects and rehabilitation following pediatric brain tumor.* J Pediatr Rehabil Med, 2011. **4**(1): p. 47-58.
 37. Robinson, K.E., Kuttesch, J. F., Champion, J. E., Andreotti, C. F., Hipp, D. W., Bettis, A., et al., *A quantitative meta-analysis of neurocognitive sequelae in survivors of pediatric brain tumors.* Pediatr Blood Cancer, 2010. **55**(3): p. 525-31.
 38. Mulhern, R.K., Palmer, S. L., Reddick, W. E., Glass, J. O., Kun, L. E., Taylor, J., et al., *Risks of young age for selected neurocognitive deficits in medulloblastoma are associated with white matter loss.* J Clin Oncol, 2001. **19**(2): p. 472-9.
 39. Spiegler, B.J., Bouffet, E., Greenberg, M. L., Rutka, J. T., & Mabbott, D. J., *Change in neurocognitive functioning after treatment with cranial radiation in childhood.* J Clin Oncol, 2004. **22**(4): p. 706-13.
 40. Oleiro, M., *Back to School, Back to Normal? Exploring the Lived Experiences of Childhood Cancer Survivors and their Families Throughout the School Re-Entry Process,* in *Department of Child and Youth Studies* 2013, Brock University.
 41. Zebrack, B.J., Gurney, J. G., Oeffinger, K., Whitton, J., Packer, R. J., Mertens, A., et al., *Psychological outcomes in long-term survivors of childhood brain cancer: a report from the childhood cancer survivor study.* J Clin Oncol, 2004. **22**(6): p. 999-1006.
 42. Fuemmeler, B.F., T.D. Elkin, and L.L. Mullins, *Survivors of childhood brain tumors: behavioral, emotional, and social adjustment.* Clin Psychol Rev, 2002. **22**(4): p. 547-85.
 43. Rey-Casserly C, P.S., *Emotional adjustment, leadership, and depressive symptoms among adolescent survivors of brain tumors,* in *Psychosocial and Neurocognitive Consequences of Childhood*

Cancer: a Symposium in Tribute to Raymond K Mulhern 2006: Memphis, TN.

44. D'Agostino, N.M. and K. Edelstein, *Psychosocial challenges and resource needs of young adult cancer survivors: implications for program development*. J Psychosoc Oncol, 2013. **31**(6): p. 585-600.
45. Eilertsen, M.E., Rannestad, T., Indredavik, M. S., & Vik, T., *Psychosocial health in children and adolescents surviving cancer*. Scand J Caring Sci, 2011. **25**(4): p. 725-34.
46. Reinfjell, T., Lofstad, G. E., Veenstra, M., Vikan, A., & Diseth, T. H., *Health-related quality of life and intellectual functioning in children in remission from acute lymphoblastic leukaemia*. Acta Paediatr, 2007. **96**(9): p. 1280-5.
47. Fouladi, M., Gilger, E., Kocak, M., Wallace, D., Buchanan, G., Reeves, C., et al., *Intellectual and functional outcome of children 3 years old or younger who have CNS malignancies*. J Clin Oncol, 2005. **23**(28): p. 7152-60.
48. Merchant, T.E., Conklin, H. M., Wu, S., Lustig, R. H., & Xiong, X., *Late effects of conformal radiation therapy for pediatric patients with low-grade glioma: prospective evaluation of cognitive, endocrine, and hearing deficits*. J Clin Oncol, 2009. **27**(22): p. 3691-7.
49. Reimers, T.S., Mortensen, E. L., Nysom, K., & Schmiegelow, K., *Health-related quality of life in long-term survivors of childhood brain tumors*. Pediatr Blood Cancer, 2009. **53**(6): p. 1086-91.
50. Hudson, M.M., Mertens, A. C., Yasui, Y., Hobbie, W., Chen, H., Gurney, J. G., et al., *Health status of adult long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor Study*. JAMA, 2003. **290**(12): p. 1583-92.
51. Bhatia, S., Goodwin, T. L., Burwinkle, T. M., Lansdale, M. F., Dahl, G. V., Huhn, S. L., et al., *High risk of subsequent neoplasms continues with extended follow-up of childhood Hodgkin's disease: report from the Late Effects Study Group*. J Clin Oncol, 2003. **21**(23): p. 4386-94.
52. Neglia, J.P., Friedman, D. L., Yasui, Y., Mertens, A. C., Hammond, S., Stovall, M., et al., *Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study*. J Natl Cancer Inst, 2001. **93**(8): p. 618-29.
53. Lipshultz, S.E., Lipsitz, S. R., Mone, S. M., Goorin, A. M., Sallan, S. E., Sanders, S. P., et al., *Female sex and drug dose as risk factors*

- for late cardiotoxic effects of doxorubicin therapy for childhood cancer.* N Engl J Med, 1995. **332**(26): p. 1738-43.
54. Waber, D.P., Tarbell, N. J., Fairclough, D., Atmore, K., Castro, R., Isquith, P., et al., *Cognitive sequelae of treatment in childhood acute lymphoblastic leukemia: cranial radiation requires an accomplice.* J Clin Oncol, 1995. **13**(10): p. 2490-6.
 55. Melin, A.E., Adan, L., Leverger, G., Souberbielle, J. C., Schaison, G., & Brauner, R., *Growth hormone secretion, puberty and adult height after cranial irradiation with 18 Gy for leukaemia.* Eur J Pediatr, 1998. **157**(9): p. 703-7.
 56. Oeffinger, K.C., Mertens, A. C., Sklar, C. A., Yasui, Y., Fears, T., Stovall, M., et al., *Obesity in adult survivors of childhood acute lymphoblastic leukemia: a report from the Childhood Cancer Survivor Study.* J Clin Oncol, 2003. **21**(7): p. 1359-65.
 57. McDougall, J. and M. Tsonis, *Quality of life in survivors of childhood cancer: a systematic review of the literature (2001-2008).* Support Care Cancer, 2009. **17**(10): p. 1231-46.
 58. Zebrack, B.J. and W. Landier, *The perceived impact of cancer on quality of life for post-treatment survivors of childhood cancer.* Qual Life Res, 2011. **20**(10): p. 1595-608.
 59. Klassen, A.F., Anthony, S. J., Khan, A., Sung, L., & Klaassen, R., *Identifying determinants of quality of life of children with cancer and childhood cancer survivors: a systematic review.* Support Care Cancer, 2011. **19**(9): p. 1275-87.
 60. Korinthenberg, R., Neuburger, D., Nikkhah, G., Teske, C., Schnabel, K., & Calaminus, G., *Assessing quality of life in long-term survivors after (1)(2)(5)l brachytherapy for low-grade glioma in childhood.* Neuropediatrics, 2011. **42**(3): p. 110-5.
 61. Langeveld, N.E., Grootenhuys, M. A., Voute, P. A., de Haan, R. J., & van den Bos, C., *Quality of life, self-esteem and worries in young adult survivors of childhood cancer.* Psychooncology, 2004. **13**(12): p. 867-81.
 62. Ganz, P.A., *Late effects of cancer and its treatment.* Semin Oncol Nurs, 2001. **17**(4): p. 241-8.
 63. Macartney, G., Harrison, M. B., Vandenberg, E., Stacey, D., & McCarthy, P., *Quality of life and symptoms in pediatric brain tumor survivors: a systematic review.* J Pediatr Oncol Nurs, 2014. **31**(2): p. 65-77.
 64. Zebrack, B.J. and M.A. Chesler, *Quality of life in childhood cancer survivors.* Psychooncology, 2002. **11**(2): p. 132-41.

65. Recklitis, C.J., Diller, L. R., Li, X., Najita, J., Robison, L. L., & Zeltzer, L., *Suicide ideation in adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study*. J Clin Oncol, 2010. **28**(4): p. 655-61.
66. Feldman, B.M., Grundland, B., McCullough, L., & Wright, V., *Distinction of quality of life, health related quality of life, and health status in children referred for rheumatologic care*. J Rheumatol, 2000. **27**(1): p. 226-33.
67. Berra, S., Ravens-Sieberer, U., Erhart, M., Tebe, C., Bisegger, C., Duer, W., et al., *Methods and representativeness of a European survey in children and adolescents: the KIDSCREEN study*. BMC Public Health, 2007. **7**: p. 182.
68. WHO, *Introduction, Administration, Scoring and Generic Version of the Assessment*, in *WHOQOL-BREF1996*, World Health Organization: Genova.
69. Varni, J.W., T.M. Burwinkle, and M.M. Lane, *Health-related quality of life measurement in pediatric clinical practice: an appraisal and precept for future research and application*. Health Qual Life Outcomes, 2005. **3**: p. 34.
70. Matza, L.S., Swensen, A. R., Flood, E. M., Secnik, K., & Leidy, N. K., *Assessment of health-related quality of life in children: a review of conceptual, methodological, and regulatory issues*. Value Health, 2004. **7**(1): p. 79-92.
71. Blaauwbroek, R., Stant, A. D., Groenier, K. H., Kamps, W. A., Meyboom, B., & Postma, A., *Health-related quality of life and adverse late effects in adult (very) long-term childhood cancer survivors*. Eur J Cancer, 2007. **43**(1): p. 122-30.
72. Meeske, K.A., Patel, S. K., Palmer, S. N., Nelson, M. B., & Parow, A. M., *Factors associated with health-related quality of life in pediatric cancer survivors*. Pediatr Blood Cancer, 2007. **49**(3): p. 298-305.
73. Zeltzer, L.K., Recklitis, C., Buchbinder, D., Zebrack, B., Casillas, J., Tsao, J. C., et al., *Psychological status in childhood cancer survivors: a report from the Childhood Cancer Survivor Study*. J Clin Oncol, 2009. **27**(14): p. 2396-404.
74. Ribí, K., Relly, C., Landolt, M. A., Alber, F. D., Boltshauser, E., & Grotzer, M. A., *Outcome of medulloblastoma in children: long-term complications and quality of life*. Neuropediatrics, 2005. **36**(6): p. 357-65.

75. Palmer, S., Mitchell, A., Thompson, K., & Sexton, M., *Unmet needs among adolescent cancer patients: a pilot study*. Palliat Support Care, 2007. **5**(2): p. 127-34.
76. Maddrey, A.M., Bergeron, J. A., Lombardo, E. R., McDonald, N. K., Mulne, A. F., Barenberg, P. D., & Bowers, D. C., *Neuropsychological performance and quality of life of 10 year survivors of childhood medulloblastoma*. J Neurooncol, 2005. **72**(3): p. 245-53.
77. Aarsen, F.K., Paquier, P. F., Reddingius, R. E., Streng, I. C., Arts, W. F., Evera-Preesman, M., & Catsman-Berrevoets, C. E., *Functional outcome after low-grade astrocytoma treatment in childhood*. Cancer, 2006. **106**(2): p. 396-402.
78. Pompili, A., Caperle, M., Pace, A., Ramazzotti, V., Raus, L., Jandolo, B., & Occhipinti, E., *Quality-of-life assessment in patients who had been surgically treated for cerebellar pilocytic astrocytoma in childhood*. J Neurosurg, 2002. **96**(2): p. 229-34.
79. Zuzak, T.J., Poretti, A., Drexel, B., Zehnder, D., Boltshauser, E., & Grotzer, M. A., *Outcome of children with low-grade cerebellar astrocytoma: long-term complications and quality of life*. Childs Nerv Syst, 2008. **24**(12): p. 1447-55.
80. Gerber, N.U., Zehnder, D., Zuzak, T. J., Poretti, A., Boltshauser, E., & Grotzer, M. A., *Outcome in children with brain tumours diagnosed in the first year of life: long-term complications and quality of life*. Arch Dis Child, 2008. **93**(7): p. 582-9.
81. Wilson, I.B. and P.D. Cleary, *Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes*. JAMA, 1995. **273**(1): p. 59-65.
82. Ness, K.K., Mertens, A. C., Hudson, M. M., Wall, M. M., Leisenring, W. M., Oeffinger, K. C., et al., *Limitations on physical performance and daily activities among long-term survivors of childhood cancer*. Ann Intern Med, 2005. **143**(9): p. 639-47.
83. Stiller, C.A., *Population based survival rates for childhood cancer in Britain, 1980-91*. BMJ, 1994. **309**(6969): p. 1612-6.
84. Pang, J.W., Friedman, D. L., Whitton, J. A., Stovall, M., Mertens, A. C., Robison, L. L., & Weiss, N. S., *Employment status among adult survivors in the Childhood Cancer Survivor Study*. Pediatr Blood Cancer, 2008. **50**(1): p. 104-10.
85. Gurney, J.G., Krull, K. R., Kadan-Lottick, N., Nicholson, H. S., Nathan, P. C., Zebrack, B., et al., *Social outcomes in the Childhood*

- Cancer Survivor Study cohort*. J Clin Oncol, 2009. **27**(14): p. 2390-5.
86. Buono, L.A., Morris, M. K., Krawiecki, F. H., Norris, M. A., & al., F. e., *Evidence for the syndrome of non-verbal learning disabilities in children with brain tumors*. Child Neuropsychology, 1998. **4**: p. 144-157.
 87. Hays, D.M., Landsverk, J., Sallan, S. E., Hewett, K. D., Patenaude, A. F., Schoonover, D., et al., *Educational, occupational, and insurance status of childhood cancer survivors in their fourth and fifth decades of life*. J Clin Oncol, 1992. **10**(9): p. 1397-406.
 88. Eiser, C., Absolom, K., Greenfield, D., Snowden, J., Coleman, R., Hancock, B., & Davies, H., *Follow-up care for young adult survivors of cancer: lessons from pediatrics*. J Cancer Surviv, 2007. **1**(1): p. 75-86.
 89. Bhat, S.R., Goodwin, T. L., Burwinkle, T. M., Lansdale, M. F., Dahl, G. V., Huhn, S. L., et al., *Profile of daily life in children with brain tumors: an assessment of health-related quality of life*. J Clin Oncol, 2005. **23**(24): p. 5493-500.
 90. Parks, R., Rasch, E. K., Mansky, P. J., & Oakley, F., *Differences in activities of daily living performance between long-term pediatric sarcoma survivors and a matched comparison group on standardized testing*. Pediatr Blood Cancer, 2009. **53**(4): p. 622-8.
 91. Smith, W.A., Li, Z., Loftin, M., Carlyle, B. E., Hudson, M. M., Robison, L. L., & Ness, K. K., *Measured versus Self-reported Physical Function in Adult Survivors of Childhood Cancer*. Med Sci Sports Exerc, 2014. **46**(2): p. 211-8.
 92. Carlson, C.A., Hobbie, W. L., Brogna, M., & Ginsberg, J. P., *A multidisciplinary model of care for childhood cancer survivors with complex medical needs*. J Pediatr Oncol Nurs, 2008. **25**(1): p. 7-13.
 93. Tesouro, G.M., J.H. Rowland, and C. Lustig, *Survivorship resources for post-treatment cancer survivors*. Cancer Pract, 2002. **10**(6): p. 277-83.
 94. Ness, K.K., Hudson, M. M., Ginsberg, J. P., Nagarajan, R., Kaste, S. C., Marina, N., et al., *Physical performance limitations in the Childhood Cancer Survivor Study cohort*. J Clin Oncol, 2009. **27**(14): p. 2382-9.
 95. Feuerstein, M., *The Journal of Cancer Survivorship: retrospective and future directions*. J Cancer Surviv, 2011. **5**(4): p. 315-9.

96. Oeffinger, K.C., P.C. Nathan, and L.C. Kremer, *Challenges after curative treatment for childhood cancer and long-term follow up of survivors*. *Pediatr Clin North Am*, 2008. **55**(1): p. 251-73, xiii.
97. Wallace, W.H., R. Anderson, and D. Baird, *Preservation of fertility in young women treated for cancer*. *Lancet Oncol*, 2004. **5**(5): p. 269-70.
98. Pötter, R., Czech, T., Dieckmann, K., Slavc, I., Wimberger-Prayer, D., & Budka, H., *Tumours of the central nervous system*. , in *Cancer in Children clinical management*, V.E.A, Editor 2005, Orxford University Press: Oxford. p. 228-254.
99. Nightingale, C.L., Quinn, G. P., Shenkman, E. A., Curbow, B. A., Zebrack, B. J., Krull, K. R., & Huang, I. C., *Health-Related Quality of Life of Young Adult Survivors of Childhood Cancer: A Review of Qualitative Studies*. *J Adolesc Young Adult Oncol*, 2011. **1**(3): p. 124-132.

APPENDIX A

Questionnaire socio-démographique

Projet de recherche
Fonctionnement dans les activités de la vie quotidienne et qualité de vie
chez les jeunes survivants de tumeurs cérébrales durant l'enfance

Code du participant: _____

Date de l'évaluation (jour/mois/année) :

<input type="text"/>	<input type="text"/>	/	<input type="text"/>	<input type="text"/>	/	<input type="text"/>	<input type="text"/>
j	j		m	m		a	a

Les questions suivantes traitent d'informations générales visant à décrire le groupe de personnes qui participe à cette étude.

1. Quelle est ta date de naissance?

<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
j	j	m	m	a	a

2. À quel genre appartiens-tu?

- ☐ Masculin
☐ Féminin

3. Quelle est ton occupation actuelle?

- ☐ À l'école, programme régulier
☐ À l'école, programme spécialisé
☐ Au travail, à temps partiel
☐ Au travail, à temps plein
☐ Au travail dans un milieu protégé ou programme insertion à l'emploi
☐ Autre (précisez) :

4. Quel est le niveau scolaire le plus élevé que tu as complété?

- ☐ 1-6^e année (école primaire)
- ☐ Secondaire 1-5 (école secondaire; non-complété)
- ☐ Diplôme d'études secondaires obtenu (DES)
- ☐ Cégep (non-complété)
- ☐ Diplôme d'études collégiales technique ou préuniversitaire obtenu (DEC)/
Études postsecondaires autre qu'universitaire
- ☐ Premier cycle universitaire
- ☐ Cycles supérieurs universitaires

5. Est-ce que tu vis :

- ☐ Avec tes parents?
- ☐ Avec ton/ ta partenaire?
- ☐ En appartement avec un ou des colocataire(s)?
- ☐ Seul(e)?

Merci pour votre temps!

APPENDIX B

CODE DU PARTICIPANT : _____

Votre santé et votre bien-être

Les questions qui suivent portent sur votre santé, telle que vous la percevez. Vos réponses permettront de suivre l'évolution de votre état de santé et de savoir dans quelle mesure vous pouvez accomplir vos activités courantes. *Merci de remplir ce questionnaire!*

Pour chacune des questions suivantes, cochez la case ☐ correspondant le mieux à votre réponse.

1. En général, diriez-vous que votre santé est :

Excellente	Très bonne	Bonne	Passable	Mauvaise
▼	▼	▼	▼	▼
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

2. Les questions suivantes portent sur les activités que vous pourriez avoir à faire au cours d'une journée normale. Votre état de santé actuel vous limite-t-il dans ces activités? Si oui, dans quelle mesure?

Mon état de santé me limite beaucoup	Mon état de santé me limite un peu	Mon état de santé ne me limite pas du tout
▼	▼	▼

- a Dans les activités modérées comme déplacer une table, passer l'aspirateur, jouer aux quilles ou au golf ☐ 1 ☐ 2 ☐ 3
- b Pour monter plusieurs étages à pied..... ☐ 1 ☐ 2 ☐ 3

CODE DU PARTICIPANT :

3. Au cours des quatre dernières semaines, combien de fois avez-vous eu l'une ou l'autre des difficultés suivantes au travail ou dans vos autres activités quotidiennes à cause de votre état de santé physique?

	Tout le temps	La plupart du temps	Parfois	Rarement	Jamais
a. Avez-vous accompli moins de choses que vous l'auriez voulu?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
b. Avez-vous été limité(e) dans la nature de vos tâches ou de vos autres activités?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

4. Au cours des quatre dernières semaines, combien de fois avez-vous eu l'une ou l'autre des difficultés suivantes au travail ou dans vos autres activités quotidiennes à cause de l'état de votre moral (comme le fait de vous sentir déprimé(e) ou anxieux(se))?

	Tout le temps	La plupart du temps	Parfois	Rarement	Jamais
a. Avez-vous accompli moins de choses que vous l'auriez voulu?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
b. Avez-vous fait votre travail ou vos autres activités avec moins de soin qu'à l'habitude?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

5. Au cours des quatre dernières semaines, dans quelle mesure la douleur a-t-elle nui à vos activités habituelles (au travail comme à la maison)?

Pas du tout	Un peu	Moyennement	Beaucoup	Énormément
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

CODE DU PARTICIPANT :

6. Ces questions portent sur les quatre dernières semaines. Pour chacune des questions suivantes, donnez la réponse qui s'approche le plus de la façon dont vous vous êtes senti(e). Au cours des quatre dernières semaines, combien de fois...

	Tout le temps	La plupart du temps	Parfois	Rarement	Jamais
a vous êtes-vous senti(e) calme et serein(e)?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
b avez-vous eu beaucoup d'énergie?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
c vous êtes-vous senti(e) triste et démoralisé(e)?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

7. Au cours des quatre dernières semaines, combien de fois votre état physique ou moral a-t-il nui à vos activités sociales (comme visiter des amis, des parents, etc.)?

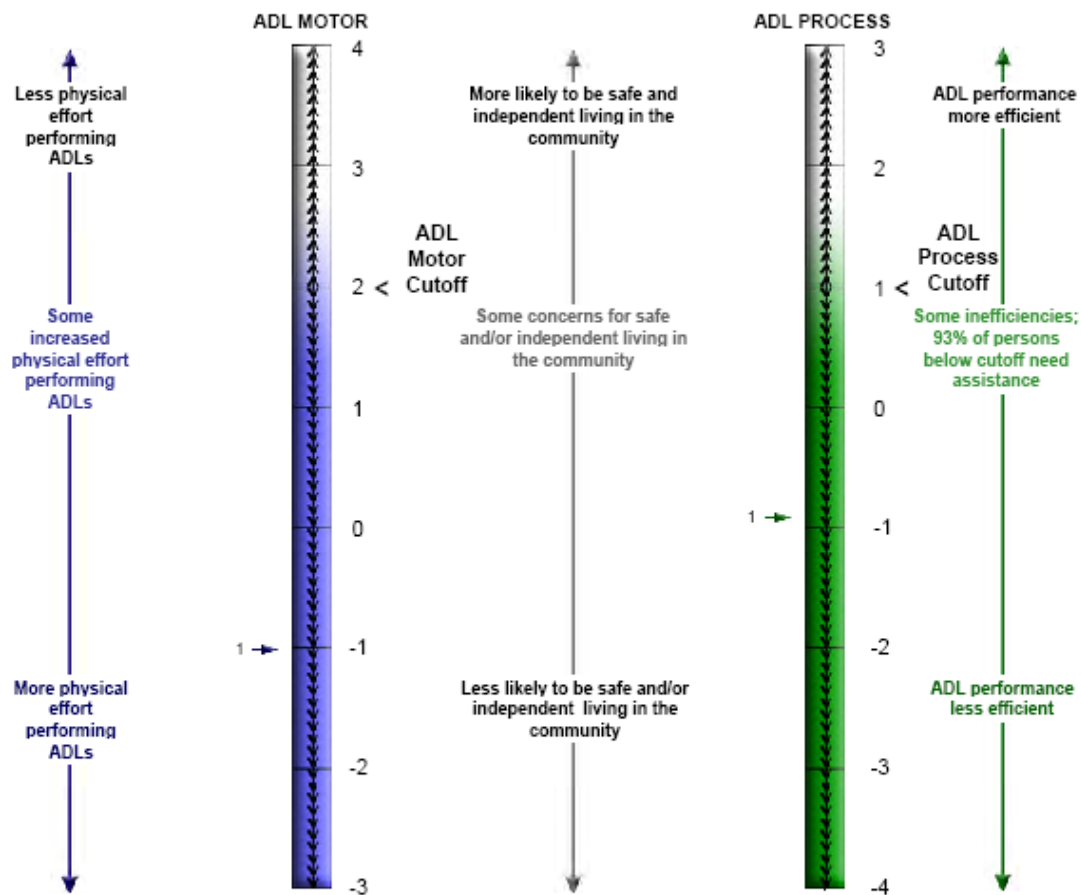
Tout le temps	La plupart du temps	Parfois	Rarement	Jamais
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

Merci d'avoir bien voulu répondre à ces questions!

APPENDIX C

ASSESSMENT OF MOTOR AND PROCESS SKILLS (AMPS) GRAPHIC REPORT

Client:	Jordon V	DATE	MOTOR	PROCESS
Occupational therapist:	AMPS Faculty	Evaluation 1 06/30/2005	-0.95	-0.83



The numbers on the ADL motor and ADL process scales are units of ADL ability (logits). The results are reported as ADL motor and ADL process measures plotted in relation to the AMPS scale cutoffs. Measures below the cutoffs indicate that there was diminished quality or effectiveness of performance of instrumental and/or personal activities of daily living (ADL). See the AMPS Narrative Report for further information regarding the interpretation of a single AMPS evaluation.

APPENDIX D



CHU Sainte-Justine
*Le centre hospitalier
universitaire mère-enfant*

Pour l'amour des enfants

FORMULAIRE D'INFORMATION ET DE CONSENTEMENT



1. Titre du projet de recherche

Fonctionnement dans les activités de la vie quotidienne et qualité de vie chez les jeunes survivants de tumeur cérébrale durant l'enfance.

2. Nom des chercheurs

Chercheur responsable du projet au CHU Sainte-Justine

Catherine Demers, candidate à la M.Sc., ergothérapeute

Collaborateurs internes et externes

Isabelle Gélinas, Ph.D., Université McGill

Anne-Sophie Carret, MD, CHU Ste-Justine

Marie St-Jacques, infirmière de recherche, CHU Ste-Justine

3. Source de financement

Ce projet est financé par la Fondation Coast-to-Coast.

4. Invitation à participer à un projet de recherche

Le département d'hémo/oncologie participe à des recherches dans le but d'améliorer le fonctionnement à long terme et la qualité de vie des jeunes ayant été traités durant leur enfance pour une tumeur cérébrale au CHU Ste-Justine.

Nous sollicitons aujourd'hui votre participation. Nous vous invitons à lire ce formulaire d'information afin de décider si vous êtes intéressé à participer à ce projet de recherche. Il est important de bien comprendre ce formulaire. N'hésitez pas à poser des questions. Prenez le temps nécessaire pour prendre votre décision.

5. Quelle est la nature de cette recherche ?

Grâce aux avancements dans le domaine médical, on estime présentement le taux de survie à une tumeur cérébrale diagnostiquée durant l'enfance à 70%. Toutefois, la guérison se fait parfois aux prix de séquelles importantes impliquant que plusieurs de ces survivants doivent affronter de nombreux défis lorsqu'ils parviennent à l'âge adulte. Dans ce contexte, il est important de bien comprendre les besoins de ces jeunes après leur rémission, alors qu'ils sont prêts à entreprendre leur vie de façon autonome.

L'objectif principal de cette recherche est d'évaluer l'impact à long terme de la tumeur cérébrale et des traitements au niveau du fonctionnement dans les activités quotidiennes chez les jeunes adultes survivants du cancer en comparaison avec leurs pairs. Les objectifs secondaires sont de déterminer les associations entre les difficultés notées dans les activités quotidiennes et la qualité de vie ainsi que de déterminer les facteurs associés à ces limitations.

Il s'agit d'un projet local au cours duquel nous comptons recruter environ 40 participants au CHU Ste-Justine.

6. Comment se déroulera le projet ?

Tout d'abord vous devrez remplir deux questionnaires : le premier comprenant certaines questions socio-démographiques comme votre âge et votre occupation, le deuxième comprenant des questions sur votre qualité de vie. Par la suite, vous serez observés par un ergothérapeute alors que vous effectuerez deux tâches de la vie quotidienne que vous aurez choisies.

Une seule visite est nécessaire et sera d'une durée approximative de deux heures.

Dépendamment de votre lieu de résidence et de votre préférence, l'évaluation aura lieu soit à l'hôpital Ste-Justine lors du rendez-vous annuel de suivi long terme ou à votre domicile.

L'équipe de recherche consultera votre dossier médical pour obtenir les informations pertinentes à cette recherche

7. Quels sont les avantages et bénéfices ?

Vous ne retirerez aucun avantage direct en participant à cette recherche. Toutefois, l'ergothérapeute effectuant l'évaluation fonctionnelle pourra suite à celle-ci vous donner des recommandations dans le but d'améliorer votre fonctionnement au quotidien et favoriser votre indépendance.

Ce projet permettra tout d'abord d'améliorer les connaissances au sujet des atteintes fonctionnelles à long terme causées par les tumeurs cérébrales pendant l'enfance ainsi que des besoins des jeunes survivants. Il sera également possible de cibler les déficits qui ont le plus d'impact sur votre qualité de vie. Par la suite, une meilleure connaissance de l'impact au niveau des activités de la vie quotidienne et de la qualité de vie contribuera à la mise en place d'interventions qui permettront aux jeunes survivants d'atteindre un niveau de fonctionnement optimal pour leur vie d'adulte. De plus, les résultats de cette recherche permettront de soutenir les professionnels ainsi que l'équipe médicale dans leurs interventions et prise de décision dans un but de rendre les soins et services offerts le meilleur possible.

8. Quels sont les inconvénients et les risques ?

Il n'y a aucun risque ni inconvénient physique à participer à cette recherche. Il peut cependant avoir un certain risque psychologique, soit le fait de se rappeler une expérience vécue difficile. À tout moment les participants sont encouragés à verbaliser toute difficulté ressentie avec l'évaluateur ou le chercheur principal. Il est également à considérer que la participation à cette recherche prendra de votre temps et peut impliquer du déplacement.

9. Comment la confidentialité est-elle assurée ?

Tous les renseignements obtenus sur vous pour ce projet de recherche seront confidentiels, à moins d'une autorisation de votre part ou d'une exception de la loi. Pour ce faire, ces renseignements seront codés et gardés sous clé au département d'hémo-oncologie sous la responsabilité du chercheur principal. Les questionnaires et autres données de recherche seront détruits 5 années après la fin du projet de recherche.

Cependant, aux fins de vérifier le bon déroulement de la recherche et d'assurer votre protection, il est possible qu'un délégué du comité d'éthique de la recherche du CHU Sainte-Justine consulte les données de recherche et votre dossier médical.

Par ailleurs, les résultats de cette recherche pourront être publiés ou communiqués dans un congrès scientifique mais aucune information pouvant vous identifier ne sera alors dévoilée.

10. Responsabilité

En signant ce formulaire de consentement, vous ne renoncez à aucun de vos droits prévus par la loi. De plus, vous ne libérez pas les investigateurs et le promoteur de leur responsabilité légale et professionnelle.

11. Liberté de participation

Votre participation à ce projet de recherche est libre et volontaire. Toute nouvelle connaissance susceptible de remettre en question votre décision de continuer de participer à la recherche vous sera communiquée.

Vous pouvez vous retirer de cette recherche en tout temps. Quelle que soit votre décision cela n'affectera pas la qualité des services de santé qui vous sont offerts. Les données non encore analysées seront détruites en cas de retrait de l'étude.

12. En cas de questions ou de difficultés, avec qui peut-on communiquer ?

Pour plus d'information concernant cette recherche, contactez le chercheur responsable de cette recherche au CHU Sainte-Justine :

Catherine Demers, ergothérapeute
au (514) 345-4931 poste 4568
catherine.demers@mail.mcgill.ca

Pour tout renseignement sur les droits de votre enfant à titre de participant à ce projet de recherche, vous pouvez contacter le Commissaire local aux plaintes et à la qualité des services du CHU Sainte-Justine au (514) 345-4749.

13. Consentement et assentiment

On m'a expliqué la nature et le déroulement du projet de recherche. J'ai pris connaissance du formulaire de consentement et on m'en a remis un exemplaire. J'ai eu l'occasion de poser des questions auxquelles on a répondu à ma satisfaction. Après réflexion, j'accepte de participer (18 ans ou plus) ou que mon enfant participe à ce projet de recherche. J'autorise l'équipe de recherche à consulter mon dossier médical (18 ans ou plus) ou celui de mon enfant pour obtenir les informations pertinentes à ce projet.

_____	_____	_____
Nom de l'enfant (Lettres moulées)	Assentiment de l'enfant si capable de comprendre la nature du projet) (signature)	Date

Assentiment verbal de l'enfant incapable de signer mais capable de comprendre la nature de ce projet: oui___ non___

_____	_____	_____
Nom du parent, tuteur ou du participant de 18 ans et plus (Lettres moulées)	Consentement (signature)	Date

J'ai expliqué au participant et/ou à son parent/tuteur tous les aspects pertinents de la recherche et j'ai répondu aux questions qu'ils m'ont posées. Je leur ai indiqué que la participation au projet de recherche est libre et volontaire et que la participation peut être cessée en tout temps.

_____	_____	_____
Nom de la personne qui a obtenu le consentement (Lettres moulées)	Signature	Date