

Social attainment in physically well-functioning long-term survivors of pediatric brain tumor; the role of executive dysfunction, fatigue, and psychological and emotional symptoms

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Abstract

The purpose of this cross-sectional study was to investigate long-term social attainment in physically well-functioning adult survivors of pediatric brain tumor (PBT) and identify demographic, medical, and psychological factors related to poor social outcomes, with a special focus on the significance of executive dysfunction. One hundred and fourteen PBT survivors and a healthy control group provided personal data on social outcomes, i.e., education, work, and governmental benefits, and completed questionnaires on executive function (EF), psychological and emotional difficulties, and fatigue. A significantly higher number of survivors compared to healthy controls reported having received educational adjustments and substantial government benefits, and significantly more survivors than controls were currently not engaged in regular employment/training. PBT survivors and healthy controls did not differ on educational level or living situation. The factors most strongly associated with poor social outcomes were self-reported executive dysfunction, difficulties with adaptive functioning, and fatigue. The findings show that physically well-functioning PBT survivors are at risk of poorer social outcomes and dependence on financial support in adulthood compared to their healthy peers, and underline the importance of investigating EF in short- and long-term follow-ups. Future rehabilitation efforts should focus more on compensatory strategies for executive dysfunction and improving EF skills.

Keywords: pediatric brain tumor; executive functions; social outcome; long-term; fatigue; psychological function

1. Introduction

Over the past two decades, a growing number of studies have shown that childhood cancer survivor (CCS) populations demonstrate poorer attainment than their healthy peers: lower educational levels, unemployment, financial dependence (de Boer, Verbeek, & van Dijk, 2006; Ghaderi et al., 2016; Ghaderi et al., 2013; Kunin-Batson et al., 2011; Mader, Michel, & Roser, 2017; Ness et al., 2008). Despite significant improvements in medical treatment, survivors of pediatric brain tumors (PBT) remain a particularly vulnerable subset of the CCS group (Boman, Lindblad, & Hjern, 2010; Brinkman et al., 2016; de Boer et al., 2006; Frederiksen et al., 2018; Mader et al., 2017; Ness et al., 2008).

Physical and sensory limitations, neurocognitive impairment, psychological and emotional distress, and persistent symptoms of fatigue are commonly present on completion of PBT treatment (i.e., surgery, chemotherapy and/or cranial radiation therapy [CRT]) (Brand, Chordas, Liptak, Manley, & Recklitis, 2016; Duffner, 2010; Puhr et al., 2018; Turner, Rey-Casserly, Liptak, & Chordas, 2009; Zeltzer et al., 2009). These late effects may, separately and together, hamper normal development across the lifespan, and have a cumulative negative effect on educational attainment, employment, financial independence, independent living and social relationships (Brand et al., 2016; Brinkman et al., 2016; Hocking et al., 2015; Moyer et al., 2012; Zebrack et al., 2007; Zeltzer et al., 2008).

Despite this knowledge, few studies have investigated the specific mechanisms underlying long-term socioeconomic and psychosocial outcomes in this group (Brinkman et al., 2016; de Ruiter et al., 2016), with most of the extant studies focused on sociodemographic factors, physical and sensory late effects and medical determinants (e.g., age at diagnosis and treatment type) (Frederiksen et al., 2018). For example, irradiation therapy, younger age at diagnosis, infratentorial tumor location, hydrocephalus have been identified as factors related to poorer social outcomes and quality of life (QoL), as well as certain personal characteristics, such as lower IQ, neurocognitive impairments and behavioral problems (Barrera et al., 2017; Bell, Ownsworth, Lloyd, Sheeran, & Chambers, 2018; Frederiksen et al., 2018; Robinson et al., 2015). Furthermore, it is unclear whether these studies have included PBT survivors with sensory and motor disabilities, which may impact educational and vocational goal attainment and independency. Consequently, the unique effects cognitive, psychological, and emotional problems and fatigue on long-term social attainment in this patient group are not yet well understood.

Neurocognitive impairment, and more specifically, executive function (EF), may be of particular relevance to long-term functional outcomes. EFs include attention, working

memory, processing speed, planning, problem solving, and cognitive flexibility, as well as behavioral and emotional skills such as the ability to adapt to change, monitor, and initiate, inhibit and regulate responses in accordance with situational and societal demands and expectations (Anderson, Jacobs, & Anderson, 2008, p. xxviii; Metcalfe & Mischel, 1999; Zelazo & Carlson, 2012). EFs are closely associated with frontal lobe function, but are also vulnerable to lesions in other parts of the brain, which have rich neuroanatomical connections to frontal regions (Anderson, Jacobs, & Harvey, 2008). For example, the cerebellum, the most common site for PBT, is involved in several neurocognitive functions, including EF (Moberget et al., 2015; Riva & Giorgi, 2000). Furthermore, compared to other neurocognitive skills, the developmental trajectory of EFs is prolonged, paralleling the structural maturation and remodeling of the frontal lobes spanning from infancy to young adulthood (De Luca & Leventer, 2008). This prolonged development thus creates a vulnerability to lesions at any stage of brain development. Therefore, irrespective of tumor location and age at onset, executive dysfunction is commonly seen after PBT and its treatment. However, more widespread damage to the neuronal networks underlying EFs cause greater difficulties, and early frontal lobe damage has been reported to cause a pattern of delayed onset and increase of impairments (Anderson, Jacobs, & Harvey, 2008).

There is increasing evidence that survivors of PBT have problems with both cognitive and behavioral aspects of EF, and that disruptions to EF maturation may have detrimental consequences for social-emotional competence, adaptive functioning, and academic and vocational achievement (Beauchamp & Anderson, 2010; de Ruiter et al., 2016; Koustenis, Hernaiz Driever, de Sonnevill, & Rueckriegel, 2016; Puhr et al., 2018; Riggs, B. Jahromi, Razza, E. Dillworth-Bart, & Mueller, 2006; Wolfe, Madan-Swain, & Kana, 2012; Wolfe, Vannatta, Nelin, & Yeates, 2015; Wolfe et al., 2013).

Executive dysfunction has been linked to impairments in self-awareness in several childhood brain injury populations, including PBT survivors (Krasny-Pacini et al., 2015; McCurdy et al., 2016). Studies have found that PBT survivors underestimate peer relationship difficulties, and overestimate their own EF skills (Devine et al., 2016; McCurdy et al., 2016), possibly due to diminished levels of self-awareness (Sølsnes, Skranes, Brubakk, & Løhaugen, 2014). Impairments in self-awareness may prevent an individual from identifying and applying necessary compensatory strategies, thereby delaying rehabilitation progress, and consequently interrupting educational and vocational opportunities (Shames, Treger, Ring, & Giaquinto, 2007).

Due to its complex and dynamic nature, executive dysfunction may remain undetected by professionals, and is often misinterpreted, e.g., as negative volitional aspects dependent on the individual's character and psychological functioning (Anderson, Anderson, Jacobs, & Smith, 2010; Lezak, Howieson, Bigler, & Tranel, 2012). Understanding EF and the related underlying mechanisms of poor long-term social attainment is crucial to prevent social inequity for survivors of PBT. This knowledge would provide a foundation for advising health and education professionals on appropriate intervention strategies.

The main purpose of this study was to investigate social outcomes in a group of young, physically well-functioning adult survivors of PBT compared to a group of healthy controls, and to examine how self-reports of executive dysfunction, psychological and emotional problems, and fatigue are related to less favorable social outcomes. Based on existing literature, we hypothesized that PBT survivors, despite the absence of serious physical debilitations, would report lower educational levels, a greater need for societal support (i.e., educational adjustments, vocational measures, government benefit uptake), and less optimal employment/training status compared to the healthy control group. We also aimed to extend our previous work showing higher levels of self-reported executive dysfunction, psychological and emotional problems and fatigue in PBT survivors compared to healthy peers (Puhr et al., 2018), by exploring the association between these variables and social attainment in the PBT survivor group. We expected problems in these domains to be associated to less favorable social outcomes, but most importantly, with executive dysfunction making the largest contribution. Finally, we investigated the role of tumor- and treatment-related factors. Based on the PBT literature, we expected complex treatment regimens (e.g., multiple surgeries, chemotherapy and/or CRT), younger age at diagnosis, and the presence of neurological late effects (e.g., postoperative seizures) and psychiatric comorbidity to be related to less favorable social outcomes.

2. Methods

2.1 Study participants

The study design, participants and data collection procedures have been described previously (Puhr et al., 2018). A flowchart of the study is provided (Fig. 1). Survivors of PBT were identified by The Cancer Registry of Norway fulfilling inclusion criteria defined as treatment for PBT at 0-16 years between 1990-2012, aged 18-30 at recruitment, and having completed treatment no later than 2 years prior to study participation. Exclusion criteria included self-reported severe difficulties with activities of daily life (ADL), self-reported

severe sensory and motor disabilities, and pre-tumor cognitive/neurological deficits due to non-tumor diagnoses, evidenced in patient records.

In May 2015, 312 eligible PBT survivors received self-report forms by mail to assess social outcomes and need for support (i.e., educational and occupational status and need for educational/occupational adjustments and/or government benefits), EF, psychological and emotional functioning, and fatigue. Eligible participants with sensory impairments and physical disabilities seriously interfering with everyday functioning were not required to respond. Of the 312 PBT survivors, 12 were excluded due to treatment for recurrent/residual tumor within last two years, and five because of pre-tumor cognitive/neurological problems due to non-tumor diagnoses. One hundred and fourteen of 295 (38.6%) PBT survivors completed the self-report questionnaires. All PBT participants reported normal or close to normal sensory and/or motor function. Mean age at onset was 9.4 years (range: 0.5-17.0, SD=4.43) and mean time since treatment completion was 13.9 years (range=2.6-25.1, SD=5.61). No age differences were found between PBT survivors who did and did not participate in the study ($t=.72$, $p=.472$), but more females participated in the study ($\chi^2=7.05$, $p=.008$).

Clinical characteristics are presented in Table 1. Information on tumor histology, location, age at diagnosis and type of treatment was gathered from patient records, and the third version of the International Classification of Childhood Cancer (ICCC-3) was used to classify participants into larger diagnostic subgroups. CRT, chemotherapy, hormone replacement treatment (i.e., growth hormones, cortisol, thyroid stimulating hormones, testosterone and estrogen, or antidiuretic hormones), postoperative seizures (i.e., ≥ 1 seizure after tumor surgery), postoperative hydrocephalus treatment (ventriculoatrial shunt, ventriculoperitoneal shunt or third ventriculostomy), and psychiatric comorbidity (i.e., as classified by the International Classification of Disease -10 codes F01-F99) was registered as yes/no.

A healthy control group matched for age and sex was recruited from The National Population Register of Norway and received self-report forms identical to those of the patient group. Of the 868 controls invited, 170 returned the completed self-report form (19.6 %).

2.2 Social outcome variables

In addition to self-report forms on psychological and emotional functioning, EF and fatigue, participants in both groups provided the following personal data; living situation (i.e., either living independently or with parents/caregivers), educational level (i.e., years and

highest attained degree), educational adjustments, employment/training status and government benefit uptake. Educational adjustments were coded as yes/no, “yes” referred to contact with educational and psychological counselling services, additional educational adjustment or support in school/higher education (e.g., individual development plan, individual curriculum, studying in small groups, help from a special education teacher) and/or technical aids. Employment/training status was coded as yes/no as to whether or not the participants were engaged in regular work, studies or military service. Participants who reported being unemployed or working/studying, but receiving vocational measures, Work Assessment Allowance (WAA), disability pension and/or daily cash benefits in case of sickness were registered as not being engaged in regular work, studies or military service. Government benefit uptake was coded as yes/no as to whether or not participants were receiving substantial government benefits, such as WAA, disability pension, unemployment benefit or financial assistance.

(Insert Table 1 about here)

2.3 Questionnaires for self-reported executive function, psychological and emotional difficulties and fatigue

BRIEF-A. For surveying EF in everyday activities over the past 6 months, the Behavior Rating Inventory of Executive Function - Adult Version (BRIEF-A; Roth et al., 2005) was employed. The BRIEF-A contains 75 items rated on a three-point scale (1=never; 2=sometimes; 3=often) and three indices are generated: Behavior Regulation Index (BRI; including subscales Inhibit, Shift, Emotional Control, and Self-Monitor), Metacognitive Index (MI; including subscales Initiate, Working Memory, Plan/Organize, Task Monitor, and Organization of Materials) and a Global Executive Composite (GEC). The BRIEF-A had high levels of internal consistency; Cronbach’s alpha of $=.97$ and $=.96$ for the patient and control group, respectively. No BRIEF-A protocols were excluded due to validity problems, but three protocols were excluded because of elevated scores on the Inconsistency scale.

SCL-90-R. The Symptom Checklist-90-Revised (SCL-90-R; Derogatis, 1994) was used to assess presence and severity of psychological symptoms during the past week. The SCL-90-R is a 90-item questionnaire using a 5-point Likert scale (0 - 4). The items generate nine symptom scales; Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism, and a

measure of global symptom severity (Global Severity Index; GSI). The SCL-90-R showed high internal consistency for both patient and control groups; Cronbach's alpha of $=.98$ for both groups.

ASR. The Adult Self-Rating (ASR) from the Achenbach System of Empirically Based Assessment (ASEBA; Achenbach & Rescorla, 2003) was used to assess self-reported emotional and behavioral problems. One hundred and twenty-six items are rated on a three-point scale (0 = statement not true; 1 = statement sometimes true; 2 = statement very true). From these 126 items, eight syndrome scales are generated; Anxious/Depressed, Withdrawn, Somatic Complaints, Thought Problems, Attention Problems, Aggressive Behavior, Rule-Breaking Behavior, and Intrusive Behavior. Three composite scores are produced; Total Problems, Internalizing Problems (sum of the scales anxious/depressed, withdrawn, and somatic complaints), and Externalizing Problems (sum of the scales aggressive, rule-breaking, and intrusive behavior). In addition to the ASR syndrome scales, we included the Adaptive Functioning subscale, which contains 38 items relating to friends, spouse or partner, family, education, and work. Internal consistency for the ASR was high; Cronbach's alpha of $=.97$ and $=.96$ for the patient group and control group for the ASR, respectively.

FQ. The Fatigue Questionnaire (FQ; Chalder et al., 1993) was employed to measure mental and physical fatigue severity. The FQ contains 11 items reflecting mental fatigue (MF; 4 items) and physical fatigue (PF; 7 items) for the last month, with the total fatigue score (TF) representing the sum of these scale scores. Items are rated from 0 ("less than usual") to 3 ("much more than usual"). In addition, two items are scored on the duration of the symptoms (0 = "less than a week", 3 = "6 months or more"). In order to define fatigue caseness/chronic fatigue, a dichotomized score (0, 0, 1, 1) is used, where a dichotomized sum score of ≥ 4 with a duration of ≥ 6 months classifies as fatigue caseness (Loge, Ekeberg, & Kaasa, 1998). Cronbach's alpha of $=.90$ showed a high level of internal consistency for the FQ scale for both the patient and control group.

2.4 Data analyses

Statistical analyses were conducted using the statistical package SPSS for Windows, version 25.0 (SPSS, Inc., Chicago, Illinois). Missing item scores were replaced by the participant's average subscale score where at least 2/3 of the items were completed (Tabachnick & Fidell, 2007). Due to non-normally distributions, non-parametric statistics

were conducted. Between group and subgroup differences were tested by Pearson Chi Square and Mann-Whitney *U* test. Bonferroni corrections for multiple comparisons were employed; only differences surviving corrections are reported. Effect size (ES) is reported as *r* for continuous data and as ϕ for categorical data, in both cases defining small ES as $=.1 - .3$; medium ES as $=.3-.5$; large ES as $>.5$ (Field, 2009).

The social outcome variables on which significant between group differences were found were retained for univariate and logistic regression analyses within the PBT survivor group. Variables potentially associated with social outcomes included questionnaire subscales and demographic (age, sex, education, time since treatment completion), tumor-related (age at diagnosis, location [supra- vs infratentorial], tumor type), treatment-related (standard treatment [single surgery only] vs. complex treatment regimens [multiple surgeries, CRT treatment, chemotherapy, and/or hormone therapy]) and late effect variables (neurological late effects [postoperative hydrocephalus, history of postoperative seizures], and psychiatric comorbidity).

The questionnaires for which there were significant differences between the various social outcome subgroups of PBT survivors, were retained as variables potentially associated with social outcomes. For questionnaires, there was a substantial problem of multicollinearity. For this reason, the Forward Likelihood Ratio (LR) was used to identify subscale scores significantly associated with outcome variables. Age and educational level were entered as covariates in the logistic regression models for those self-report measures that proved significant in univariate analyses. Univariate logistic regression analyses were used to screen for significant demographic, tumor-related, treatment-related and late effect variables (i.e., variables $p < .20$) for entry into the multi-variable models for social outcomes. The logistic regression models' goodness-of-fit was assessed by using the Hosmer and Lemeshow (H-L) test. A *p*-value of .05 or higher of the H-L test would indicate that the model fitted well with the data. All reported *p*-values and 95% confidence intervals are two-sided.

2.5 Compliance with ethical standards

The study was approved by the Regional Committee for Medical Research Ethics in South Eastern Norway (REC South East; 2014/379), and was conducted in accordance with the Declaration of Helsinki by the World Medical Association Assembly. Following a complete description of the study, written informed consent was obtained from all individual participants included in the study.

3. Results

3.1 Social outcomes in PBT survivors compared to controls

Healthy controls and PBT survivors did not differ on distribution of sex, educational level or living situation (all $ps > .05$) (Table 1). PBT survivors were more likely to receive educational adjustments ($p < .001$), not engage in regular employment/training ($p < .001$), and previously and/or currently receive substantial government benefits ($p < .001$), (Table 1).

Between group differences on self-reported EF, psychological, and emotional problems, and fatigue are summarized, as these have been presented previously (Puhr et al., 2018), and are displayed in detail in Supplementary Table 1. The PBT group recorded higher scores than controls on: the SCL-90-R Global Scale Index (GSI) and the subscales Obsessive-Compulsive, Interpersonal Sensitivity, and Hostility ($p = .001-.002$, $r = .18-.30$); the ASR subscales Somatic Complaints, Thought Problems, Attention Problems, Rule-Breaking Behavior, composite scales, and Total Problems ($p > .001-.003$, $r = .18-.25$); the BRIEF-A subscales Shift, Self-Monitor, Initiate, Working Memory, and Plan/Organize, and the composite scales indexing behavioral (BRI) and metacognitive (MI) aspects of EF, as well as the Global Executive Composite score (GEC) ($p > .001-.002$, $r = .1-.30$); and the FQ mental fatigue (MF) subscale ($p = .005$, $r = .17$).

3.2 Self-report measures related to social outcomes and need for support in PBT survivors

There were significant differences on all self-report measures between the PBT survivors who had received educational adjustments, who were not currently engaged in regular employment/training, who had received substantial government benefits reported significantly and those who did not have these issues ($p < .001-.004$, $r = .23-.41$, see Table 2). All subscales from each of the self-report measures were therefore retained as variables potentially related to social outcomes. Separate logistic regression analyses were performed for each self-report instrument individually, and the results from these models are provided in Table 3. H-L tests indicated a good fit for the models (all $p > .05$).

Higher scores on the subscales Obsessive-Compulsive (SCL-90-R), Attention Problems (ASR), Working Memory (BRIEF-A) and Mental Fatigue (FQ) and lower scores on the subscale Hostility (SCL-90-R) were related to higher odds of having received educational adjustments (Table 3). Lower scores on the subscales Phobic Anxiety (SCL-90-R), Initiate (BRIEF-A) and Physical Fatigue (FQ) and a higher score on the ASR subscale Adaptive Functioning subscale (i.e., higher level of adaptive functioning) were related to higher odds of

being engaged in regular employment/training (Table 3). Higher scores on the subscales Obsessive-Compulsive (SCL-90-R), Initiate (BRIEF-A), Physical Fatigue (FQ) and lower scores on the subscale Adaptive Functioning (ASR) were related to higher odds of substantial government benefit uptake (Table 3).

(Insert Table 2 and 3 about here)

3.3 Demographic and tumor- and treatment-related variables and late effects related to social outcomes and need for support in PBT survivors

Results from the logistic regression models are provided in Table 4. H-L tests indicated a good fit for the models (all $p > .05$). For educational adjustments in the PBT survivor group, educational level, treatment type, and psychiatric comorbidity remained as potentially associated variables, but only treatment type was statistically significant, $p = .003$, indicating that complex treatment regimens combining multiple surgeries, chemotherapy, CRT and/or hormone therapy is significantly associated with receiving educational adjustments (Table 4). Age, educational level, psychiatric comorbidity, and treatment type remained as potentially associated variables for employment/training status in PBT survivors, of which three were significant; treatment type ($p = .007$), educational level ($p = .020$), and age ($p = .045$) indicating that standard treatment, higher educational level and lower current age was related to higher odds of being engaged in regular employment/training (Table 4). Age, educational level, treatment type, and psychiatric comorbidity remained as potentially associated variables for government benefit uptake, and all four variables were statistically significant, showing that having received complex treatment regimens ($p < .001$), presence of psychiatric comorbidity ($p = .014$), higher age ($p = .007$), and lower educational level ($p = .009$) increased the odds of substantial government benefit uptake (Table 4).

(Insert Table 4 about here)

4. Discussion

The present study of social outcomes in physically well-functioning PBT survivors has three main findings. First, we found higher rates of PBT survivors compared to healthy controls who reported having received educational adjustments and substantial government benefits, and who were currently not engaged in regular employment/training. Second, across most of the administered questionnaires, those factors most strongly related to poor social

outcomes were subscales measuring self-reported executive dysfunction, difficulties with adaptive functioning and fatigue. Third, complex treatment regimen (i.e., multiple surgeries, chemotherapy, CRT, and/or hormone therapy) was significantly associated with overall poorer social outcomes, and the presence of post-treatment psychiatric comorbidity was significantly related to government benefit uptake.

Consistent with the literature on social outcomes in CCS populations, and the few studies that exist on PBT survivors specifically, our findings show that this CCS subgroup have substantially more difficulties than their healthy peers in negotiating important adult milestones such as being engaged in regular employment or training and being financially independent (Boman et al., 2010; Brinkman et al., 2016; de Boer et al., 2006; Frederiksen et al., 2018; Mader et al., 2017; Ness et al., 2008). As PBT survivors with severe difficulties with activities of daily life (ADL) and sensory and motor disabilities were excluded from this study, our findings also show that it is not only medical late effects and physical disabilities that hinder PBT survivors from success in education, work and financial independency, but that also psychological and psychosocial aspects are important for socioeconomic outcomes. However, the findings from this study also show some encouraging outcomes; the PBT survivors did not differ from the healthy controls with respect to educational level or living situation, i.e. living independently or with parents/caregivers. Also, although there is a difference between the groups in activity status, it is worth noting that more PBT survivors than not were currently engaged in regular work, studies or military service. However, similar educational levels in both groups is most likely a reflection of the equality of the Norwegian welfare and educational system, as all inhabitants are entitled to education at a high school level, and educational services and adjustments are offered to all students who are struggling academically. Therefore, it seems that problems arise as they gradually leave the support of caregivers and the educational system, and enter adulthood, facing the demands of independency that this transition entails. Moreover, due to the relatively young age in our sample, it is plausible that participants in both groups are likely to not yet have established an independent living situation, e.g., for financial reasons. This particular social outcome could therefore benefit from being monitored further.

Our findings demonstrate that cognitive and executive dysfunction are more strongly associated to poorer social outcomes in this group PBT survivors, with emotional and psychological distress less impactful. Specifically, aspects of EF (e.g., problems with attention, working memory, and the ability to initiate activity) were significantly associated with educational adjustments and substantial government benefits, and reduced

employment/training. Of note, OCD-symptoms also contributed to these outcomes. Review of this finding suggests that self-rating of OCD symptoms most likely reflects increased awareness of concerns regarding cognitive functioning, including executive dysfunction (Woessner & Caplan, 1995). Only one aspect of psychological and emotional distress, i.e., phobic anxiety, was significantly associated with poor employment/training status. Another factor strongly related to poor social outcomes in this study, was problems with adaptive functioning, i.e., difficulties with social relationships and problems performing efficaciously in work and/or studies.

Together, these results confirm earlier findings that disruptions to EF development may lead to serious negative functional outcomes (Ness et al., 2008; Wolfe et al., 2012; Ylvisaker & Feeney, 2008), and demonstrate the association between cognitive and behavioral aspects of executive dysfunction and academic and occupational concerns. Cognitive aspects of EF, such as attentional control, working memory, initiation, planning and organizing, selection of efficient problem-solving strategies, mental flexibility and utilization of feedback, are crucial in order to perform academic activities and workplace tasks satisfactorily (Anderson, Jacobs, & Anderson, 2008). Problems with behavioral aspects of EF (e.g., inhibition and regulation of emotional and behavioral responses), may lead to difficulties in relating to other students, colleagues and employers, which in turn may reduce subjective well-being and motivation to pursue academic and vocational goals. In a developmental perspective, intact EF is essential for the development of social competence and interpersonal skills (Beauchamp & Anderson, 2010), and several studies have found a link between various aspects of executive dysfunction and impaired social functioning and participation across different pediatric brain injury populations, including PBT survivors (Muscara, Catroppa, & Anderson, 2008; Sirois et al., 2017; Willard, Allen, Hardy, & Bonner, 2015; Wolfe et al., 2013). Similar findings have been reported also in typically developing children, such as in a study by McQuade, Murray-Close, Shoulberg, and Hoza (2013), where poor working memory was associated with social impairments such as peer rejection, poor overall social competence, and impaired conflict resolution skills.

Interestingly, PBT survivors who reported higher levels of hostility were more likely to report not having received educational adjustments. It is not unlikely that problems with higher levels of hostility may be related to problems of adaptive functioning, more specifically to difficulties with social relationships. A plausible explanation for this finding could be that PBT survivors with hostility problems may shun the help offered by education

professionals, and/or discourage education professionals from continuing to uphold supportive measures.

The results demonstrated significant differences between the PBT survivors and the controls on a majority of measures of executive dysfunction, psychological and emotional problems and physical and mental fatigue. However, although significant, these differences generally displayed small ESs, with the exception of measures of EFs, where differences were larger. These results are in contrast to the findings that this group of PBT survivors struggle significantly more with education, work and financial independency. Similar findings were reported in a study by Brinkman et al. (2016) who demonstrated severe neurocognitive impairment on performance-based measures in a large proportion of survivors of central nervous system tumors, which further was associated with lower educational attainment, unemployment and nonindependent living, yet only a few of the survivors' self-reports reflected a similar degree of cognitive and behavioral impairment in daily life.

There are several plausible explanations for this discrepancy. First, although PBT survivor self-reports yield scores within a standard deviation below the control group average, this difference is nonetheless significant, and it may be the total accumulation of subtle problems over time that translate into bigger issues of independent functioning, similar to that noted in adult survivors of pediatric traumatic brain injury (Beauchamp, Dooley, & Anderson, 2010). Second, diminished impairment awareness has been found in several childhood brain injury populations, which may often be related to executive dysfunction, and which may in part account for the close to normal levels of self-reported functioning (Krasny-Pacini et al., 2015; McCurdy et al., 2016; Sølvsnes et al., 2014). Moreover, considering that PBTs occur in the earliest years of life, survivors may habituate and gradually adapt to a subnormal level of functioning (Beauchamp et al., 2010), possibly to such a degree that it becomes their subjective normality, not necessarily perceived as impaired or different from that of their peers. Third, several studies have shown a response bias in CCS populations, i.e., a systematic tendency to underreport or deny difficulties. This bias may be related to a repressive adaptive coping style and psychological defense mechanisms (e.g., a need to be “normal” and move past the illness), subsequently resulting in an overly positive impression of outcomes (Lund, Schmiegelow, Rechnitzer, & Johansen, 2011; O’Leary, Diller, & Recklitis, 2007; Phipps, Steele, Hall, & Leigh, 2001).

Not surprisingly, complex treatment regimens and fatigue were significantly associated with poor social attainment at all three levels, whereas psychiatric comorbidity was significantly related to government benefit uptake. Interestingly, and contrary to earlier

findings, we did not find younger age at diagnosis and the presence of neurological late effects to be associated to less favorable social outcomes. However, a review of the literature by Schulte and Barrera (2010) reported contradicting evidence for the relation between age at diagnosis and social adjustment, with studies showing also either no relation between age at diagnosis and outcome, or with older age as a risk factor for poorer outcome. Thus, the relation between age at diagnosis and outcome seems to be complex. The number of participants in this study who had sustained neurological late effects, such as postoperative hydrocephalus and seizures, was relatively small, which may account for why an association to poorer social outcomes could not be found. The increased risk of debilitating late effects after PBT treatment has long been established in the literature, and the results from our study confirm earlier findings demonstrating the accumulative burden on social outcomes of having undergone combined treatment (Brinkman et al., 2016). Post-treatment fatigue is a frequent and often persisting complaint among PBT survivors, and has a negative effect on quality of life (Clanton et al., 2011; Zeltzer et al., 2009). The results from this study show furthermore that fatigue also reduces chances of favorable social attainment, as mental fatigue was significantly associated with educational adjustments, whereas physical fatigue was significantly related to less optimal employment/training status and uptake of government benefits.

The present study has several limitations, including a cross-sectional design rather than a longitudinal design, the small number of PBT survivors for the subgroup analyses of the impact of tumor- and treatment-related factors, and the relatively low PBT survivor response rate (38.6%). The relatively low response rate raises questions of the representativeness of the sample and validity of the findings. All PBT survivors in Norway fulfilling the diagnostic and age criteria were identified by The Cancer Registry of Norway, a database covering all cancer cases in Norway, and were invited to participate. This ensures a high level of representativeness. However, as the focus of our study was survivors without severe physical, sensory and motor impairments, only PBT survivors meeting the inclusion criteria defining no severe ADL, sensory and motor disabilities were asked to respond. According to earlier studies on long-term outcomes in this CCS population, performance and participation limitations are relatively frequent, and up to 26 % of adult PBT survivors report limitations in physical performance and daily activities (Ness et al., 2005). The actual target population response rate in this study may therefore be substantially higher than 38.6%, considering that up to 26 % of the original 295 invited survivors may not have met the inclusion criteria. For these reasons, it is argued that the PBT survivors that did respond

constitute a relatively representative sample of this particular PBT population. Unfortunately, an analysis of non-response bias was not possible, as data collection on non-responding participants was limited by ethical regulations, and information on physical and sensory impairments in the non-responding survivors was not available.

Another limitation to this study is that only self-report measures were employed for the exclusion criteria and for the key variables and outcomes. Considering the possibility of impaired self-awareness in this population, the reliance on self-reports may potentially have had a confounding influence on the findings. For example, it is conceivable that some PBT survivors may not have had a realistic perception of the seriousness of their physical limitations, and thus may not have met the inclusion criteria. Alternatively, due to possible impaired awareness of cognitive deficits and social functioning, the difference between the healthy control group and the PBT survivor group may in reality be greater than what the current findings have shown. Furthermore, it was not within the scope of this study to investigate coping styles, family factors (e.g., parental health, parental education and socioeconomic status, impact of PBT on family interactions), and social support in this PBT survivor group, which are all important factors that may have contributed to the observed differences.

Despite these limitations, the findings from this study provide important insights into long-term social attainment in PBT survivors and help to provide a more comprehensive picture of the underlying psychological and psychosocial mechanisms of poor social outcome in this CCS group, for which there traditionally has been limited research. These insights have important implications for long-term follow-up strategies for this patient population, and underline the importance of investigating potential executive dysfunction, both shortly after treatment completion and in a long-term perspective. In this context, rehabilitation professionals should be aware of the tendency of underreporting difficulties in this group, and that even subtle problems may gradually accumulate and cause serious negative consequences for social attainment in a lifetime perspective. Furthermore, although a majority of the PBT survivors had received educational adjustments, they nonetheless had poorer outcomes compared to their healthy peers. In light of findings from this study, to improve outcome from the educational and rehabilitation resources offered, future efforts should focus more on improving EF skills and tailoring compensatory strategies for executive dysfunction. Encouragingly, interventions aimed at improving EF in pediatric populations are rapidly emerging. However, thus far the results are mixed as to the effectiveness of current

interventions, and further research efforts are needed (Godfrey, Catroppa, Kaizar, Yeates, & Robinson, 2014; Riccio & Gomes, 2013).

In conclusion, our findings suggest that physically well-functioning PBT survivors have significant long-term problems with achieving important adult milestones such as occupational success and financial independency, and that these problems are associated with self-reports of executive dysfunction, cognitive problems, problems of adaptive functioning and mental fatigue, as well as post-treatment psychiatric comorbidity and having undergone complex treatment regimen.

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Declaration of interest statement

All authors of this article declare that they have no conflict of interest.

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