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Relationships between executive functioning and health-related quality of life in adult survivors of brain tumor and matched healthy controls

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Relationships between executive functioning and health-related quality of life in adult survivors of brain tumor and matched healthy controls

Abstract (284 words)

Introduction. Few studies have considered health-related quality of life (HRQOL) as a primary outcome measure in adult survivors of primary brain tumor (PBT), and fewer still have studied the cognitive factors that may influence it. Research suggests that executive functions (EFs) are associated with HRQOL, but there is scant evidence to support this. The present study was conducted to (1) extend prior findings about HRQOL limitations in a sample of stable, long-term adult survivors of PBT, (2) investigate the associations between objective/reported EFs and HRQOL, and (3) identify the EFs that contribute most to HRQOL.

Method. We recruited 40 survivors of PBT (> 2 years post-treatment) and 40 matched healthy controls. Participants completed an objective EF assessment (inhibition, working memory, shifting, and rule detection) and two self-report questionnaires probing EFs (Behavior Rating Inventory of Executive Function-Adult) and HRQOL (Medical Outcomes Study Short-Form 36). Participants' relatives completed observer-rated versions of these questionnaires.

Results. Patients' objective EF performances were relatively intact. However, patients and caregivers reported significantly more problems than healthy controls and their relatives, for both EFs and HRQOL. There were only negligible links between objective EFs and HRQOL, whereas numerous associations were found between reported EFs and HRQOL components. ANCOVA models revealed that specific reported EF processes contributed to both the physical and mental components of HRQOL, regardless of group.

Conclusions. From a clinical point of view, this study demonstrates that even several years after end of treatment, adult PBT survivors experience substantial problems across different HRQOL domains. HRQOL assessment should therefore be part of the long-term follow-up of PBT survivors, and clinicians should consider EF limitations when designing appropriate survivorship care plans. These findings indicate that cognitive interventions targeting EFs could improve HRQOL.

Keywords. Executive functions – Health-related quality of life – Primary brain tumor – Survivorship – Patient-reported outcomes

Introduction

Advances in primary brain tumor (PBT) treatment have led to a major improvement in patients' mean life expectancy, with a 5-year overall survival rate of 32.1% (Barnholtz-Sloan et al., 2018). Survival rates vary according to the tumor's histological subtype, but the central issue for all survivors of PBT is the quality of the survivorship experience. Regardless of tumor type, size, and location, surviving a PBT is frequently associated with long-term adverse effects (i.e., *late effects*). These encompass the physical, cognitive and psychosocial sequelae of both the tumor itself and its treatment (Panigrahy & Blüml, 2009). Late effects can emerge several years after end of treatment, and are assumed to negatively impact autonomy and health-related quality of life (HRQOL; Boele et al., 2015).

HRQOL is a multidimensional concept that covers physical, socio-emotional, and cognitive functioning (Guyatt et al., 1993). Given the frequently fatal outcome of the disease, interest in the HRQOL of patients with PBT has emerged (Klein, 2017). Relatively few studies have considered HRQOL as a primary outcome measure, and the relationship between survival and HRQOL remains poorly understood in these patients (Gabel et al., 2019). Despite this research gap, some HRQOL data are available for stable, long-term survivors of PBT (Boele et al., 2015; Dirven, et al., 2019; Lawler, 2015). However, these studies primarily concern adult survivors of pediatric PBT (e.g., Robinson, et al., 2010; Macartney, 2014; Janss, Mazewski, & Patterson, 2019). In the case of PBT in adulthood, patients seem to have poorer HRQOL than survivors of cancer with no central nervous system involvement (Boele et al., 2013). A recent meta-analysis demonstrated that patients with either meningioma or glioma may have an equally altered HRQOL (Zamanipoor Najafabadi et al., 2017). These data suggest that several years after treatment ends, and regardless of tumor type, survivors of PBT may exhibit a substantial decline in HRQOL.

As treatments improve and life expectancy increases, a shift has therefore occurred in PBT care objectives, going from survival to the preservation of an acceptable level of HRQOL for patients. For some authors, this should now be one of the primary objectives of survivorship management, as the quality of survival is at least as important as its duration (Amidei, 2018). In this vein, the next step for care is to identify and address the sequelae that may have an impact on HRQOL, so that survivors' HRQOL can ultimately be improved. A decline in HRQOL has been associated with several PBT late effects. These include physical symptoms, psychological distress, neurobehavioral changes, and cognitive deficits (Hickmann et al., 2017; Klein, 2017). One of the most serious challenges that survivors face is cognitive dysfunction, with a predominance of attention, memory, and executive deficits (Cayuela et al., 2019; Gehrke et al., 2013). *Executive functioning* refers to processes (e.g., inhibition, planning, initiation, rule detection, shifting) that are assumed to underlie behavioral adaptation and regulation in daily life (Ali et al., 2018). Executive function (EF) deficits have therefore been associated with neurobehavioral changes and are likely to impair HRQOL.

EFs can be assessed using both performance-based tasks and questionnaires (completed by patients and informants) pertaining to behavioral difficulties in daily life. Few studies have specifically focused on the assessment of executive functioning in adult survivors of PBT, be it cognitive or reported EF difficulties. Late effects have, however, been highlighted with objective EF tests of shifting, working memory, planning, and foresight. It is noteworthy that these deficits were reported in patients with a range of tumor types, grades, and treatments (Weyer-Jamora et al., 2021; see Gehrke et al., 2013, for a review). While not conducted specifically in survivors of PBT, studies undertaking ecological assessments of everyday executive functioning with questionnaires have also demonstrated difficulties in working memory, initiation, planning, and task monitoring, both in patients with high-grade glioma (Loughan et al., 2019) and in patients with meningioma or low-grade glioma (van der Linden

et al., 2020). A previous study demonstrated that adult survivors of PBT and their caregivers report more EF-related problems than healthy controls do, suggesting that EF difficulties may be encountered several years after end of treatment (Cantisano et al., 2021).

Understanding the relationship between EF deficits and HRQOL may provide useful information for improving HRQOL, enabling EF impairments to be targeted through the implementation of cognitive rehabilitation programs (Coomans, Dirven & Taphoorn, 2019). This relationship has previously been demonstrated in several populations (Cotrena et al., 2016; Mitchell et al., 2010; Stern et al., 2017), but little evidence has been collected from adult patients with PBT through objective EF assessments (Boele et al., 2014; Dutz et al., 2020; Gehring et al., 2015; Noll et al., 2017). Relationships between reported EFs and HRQOL have been demonstrated in survivors of pediatric PBT (Laffond et al., 2012; Netson et al., 2016; Ventura et al., 2018), but to the best of our knowledge, no study has so far directly attempted to examine the expected relationship between executive functioning and HRQOL in adult survivors of PBT. In addition, previous studies have shown that EFs are associated with HRQOL in healthy populations, whether they have used performance-based tasks (Davis et al., 2010; in older adults) or rating scales (Huang et al., 2020; in children). Overall, studies on this topic are scarce, in both clinical and nonclinical samples.

The present study was therefore conducted to (1) extend prior findings about impaired HRQOL in a sample of long-term adult survivors of PBT, (2) investigate the associations between objective/reported EFs and HRQOL, and (3) determine which EFs contribute most to HRQOL. As executive functioning has been shown to be linked to HRQOL in healthy populations, we decided to report data from matched healthy controls and include them in the analyses. After exploring the relationship between executive functioning and HRQOL in the entire sample, we looked at the possible influence of group membership on this relationship.

Materials and methods

This study was an observational multicentre study. It received French regulatory ethical approval (Comité de Protection des Personnes Ouest II, no. 2015/27, ID-RCB no. 2015-A01192-47) comprising International Review Board authorisation (no. NCT02693405).

Participants

Survivors of PBT ($n = 40$) were recruited within three university hospital neurosurgery departments, following a procedure described elsewhere (Cantisano et al., 2021). Participants each signed an informed consent form regarding their enrolment and the future publication of their anonymous data. Regarding inclusion criteria, patients (1) had to be aged between 20 and 59 years, to avoid the effect of normal aging on neurocognitive functioning, (2) had to have been treated (chemotherapy, radiation therapy, or surgery) for PBT, (3) had to have completed their treatment at least 2 years prior to enrolment in the study, with no recurrence of the disease, (4) had to be free of speech impairments, and (5) had to be native French speakers. Patients with brain metastases or tumors of the noncentral nervous system were excluded. Patients' eligibility regarding study criteria was verified during outpatient consultations. Medical data were obtained regarding patients' tumor type and location, along with the type of treatment received, and the time that had elapsed since the end of treatment. Given that the study protocol (self-reports) required a certain level of understanding, patients with major cognitive/comprehension impairments were excluded, based on their Mini-Mental State Examination (MMSE) score (> 24).

Healthy controls ($n = 40$) had to be aged between 20 and 59 years of age, with no history of psychiatric or neurological disorders. French had to be their native language. They were recruited via a university hospital research centre. Patients and controls were matched on age, sex, and education level. Potential participants were identified within the centre's volunteer

database and contacted by a nurse if they matched the inclusion criteria. If eligible participants gave their consent, they were enrolled in the study. Patients' medical information and participants' sociodemographic data are summarised in Table 1.

INSERT TABLE 1 ABOUT HERE

Measures

Patients' and controls' global cognitive efficiency was assessed with the MMSE). Three measures were administered to obtain objective information on EFs: (1) Stroop test (inhibition and working memory, Roussel & Godefroy, 2008), (2) Wechsler Adult Intelligence Scale Fourth Edition [(WAIS-IV, Wechsler, 2011; digit span (working memory)], and (3) French validation of the Modified Card Sorting Test (MCST; shifting, rule detection, Roussel & Godefroy, 2008).

The French version (Roy et al., 2015) of the Behavior Rating Inventory of Executive Functioning-Adult version (BRIEF-A) was used to collect reported executive functioning (patient-rated and informant-rated). This questionnaire comprises 75 items that assess the frequency of different aspects of EF-related problems. It yields a Global Executive Composite (GEC) score that can be broken down into two index scores: (1) the Behavioral Regulation Index (BRI), which encompasses four subscales (Inhibit, Shift, Emotional Control, and Self-Monitor), and (2) the Metacognition Index (MCI), which includes five subscales (Initiate, Working Memory, Plan/Organize, Task Monitor, and Organization of Materials). Raw scores are summed to obtain the various subscale and index scores, then converted into age- and sex-adjusted *t* scores (Roy et al., 2015). Higher scores indicate greater deficits.

HRQOL was assessed with the French version (Leplège et al., 1998) of the Medical Outcomes Study Short Form (SF-36) self-rated and informant-rated questionnaire. This instrument has been shown to be valid and reliable in patients with brain tumors (Bunevicius, 2017). It measures individuals' generic health status in eight dimensions: physical functioning, social functioning, role limitations (physical vs. emotional problems), bodily pain, general health, mental health, and vitality. Two composite scores can be calculated for HRQOL: (1) a physical component score (PCS), which refers to physical activities, limitations due to physical condition, perceived health, and physical pain; and (2) a mental component score (MCS), which refers to vitality, life and relationships with others, limitations due to psychological condition, and psychological health. Higher scores reflect higher levels of functioning and better health status.

Data analysis

Statistical analyses were performed using R statistical software (version 3.3.3; R Project for Statistical Computing). We conducted preliminary analyses of sociodemographic variables by comparing groups with *t* tests (quantitative variables) and χ^2 (categorical variables). Patients' and control' scores were also compared on EF variables with *t* tests. The effects of tumor type and grade were assessed by comparing subgroups of patients with Kruskal-Wallis tests.

For HRQOL data, we performed sequential analyses of covariance (Type I ANCOVAs) to examine differences between patients and matched healthy controls, with group membership as the independent variable, and SF-36 composite scores (PCS/MCS) as dependent variables, for self and informant reports. The ANCOVA was used here as an alternative to the *t* test (e.g., Borm et al., 2007). We then explored the influence of executive functioning on HRQOL, whilst controlling for the effect of group membership. Separate ANCOVAs were conducted using EF scores (objective scores, BRIEF-A BRI/MCI) as independent variables, and HRQOL scores (SF-36 PCS/MCS) as dependent variables, with group membership treated as the first covariate.

These analyses were performed for self- and informant reports on the BRIEF-A and SF-36. Beta coefficients were calculated to describe the strength and direction of the associations. Effect sizes were assessed using eta squared (η^2), which indicates the proportion of total variance accounted for by a given effect. An η^2 of 1% corresponds to a small effect, 6% is a medium effect, and 14% is a large effect (Cohen, 1988). The Bayesian information criterion (BIC; Schwarz, 1978) was used to determine the most suitable model (i.e., which EFs contributed most to HRQOL). The chosen model was the one with the lowest BIC value (Neath et al., 2012). In a third step, we added an interaction term (Group membership x Executive functioning) for each analysis, to determine whether there was an interaction effect between independent variables on the HRQOL dependent variables (PCS/MCS). ANCOVAs were conducted sequentially. Levene's test and normality checks were carried out and the assumptions were met. A p value below 0.05 was considered statistically significant.

Results

Characteristics of the groups

No differences were found between patients and healthy controls on age ($t = -0.131, p = .896$), sex ($\chi^2 = 0.503, p = .478$), or education level ($t = 0.855, p = .395$). There was also no difference between patients and controls on MMSE scores ($t = -1.41, p = .16$).

Executive data analyses

Concerning objective EF tasks (Stroop, WAIS-Digit Span subtest, MCST), patients scored significantly lower on working memory (Digit Span Backward). Regarding self- and informant-reported EFs, detailed results are described elsewhere (Cantisano et al., 2021). To summarise, patients and healthy controls differed significantly on the GEC, both for self- and informant reports. Groups also differed on self-reported MCI and informant-reported BRI. Differences almost reached significance for self-reported BRI and informant-reported MCI. Results are displayed in Table 2.

Kruskal-Wallis tests were conducted to compare scores between PBT subgroups (high-grade gliomas vs. low-grade gliomas vs. non-glioma), and to test the effects of tumor type and grade on all variables (MMSE, EF tasks, BRIEF-A, SF-36). No differences were found between the patient subgroups on any of the variables we considered.

HRQOL data analyses

ANCOVAs revealed a significant effect of group membership, with between-group differences on HRQOL self-reported PCS and MCS. Significant differences between groups were also highlighted for informant-rated HRQOL scores (all $ps < .03$; see Table 2).

ANCOVAs examining the influence of objective EF scores (Stroop total number of errors, Digit Span Forward, Digit Span Backward, MCST total number of errors) on HRQOL scores (self- and informant-reported PCS and MCS), controlling for the effect of group membership, revealed no association between these variables (all $ps > .082$), except for MCST total number of errors and self-reported PCS, $F(1, 74) = 4.849, p = .031, \eta^2 = .058$.

Regarding self-reported measures of executive functioning and HRQOL, after controlling for group membership, we observed significant effects of behavioral (BRI) and metacognitive (MCI) EF scores on both physical (PCS) and mental (MCS) HRQOL (BRI/PCS, $F(1, 74) = 10.097, p = .002$; BRI/MCS, $F(1, 74) = 18.351, p < .001$; MCI/PCS, $F(1, 74) = 11.641, p = .001$; MCI/MCS $F(1, 74) = 10.969, p = .001$). Beta coefficients, η^2 , and BIC values are displayed in Table 3. All beta coefficients were significant and negative. Eta-squared indicated medium-to-large effect sizes (11.3-18.6%). BIC values showed that the MCI model was slightly better than the BRI model when it came to explaining the PCS score, whereas the BRI model best explained the MCS score.

INSERT TABLE 3 ABOUT HERE

Concerning informant-reported measures, ANCOVAs examining the influence of BRI on PCS/MCS, controlling for group membership, revealed two associations between variables (BRI/PCS, $F(1, 58) = 5.776, p = .019$; BRI/MCS, $F(1, 58) = 12.407, p < .001$). There were also significant effects of MCI on both PCS, $F(1, 58) = 15.793, p < .001$, and MCS, $F(1, 58) = 13.906, p < .001$. Table 4 shows the beta coefficients, η^2 , and BIC values for each model. All beta coefficients were significant and negative. Eta-squared indicated medium-to-large effect sizes (8.2-19.5%). BIC values indicated that MCI was the most suitable model for explaining the PCS score. The MCI and BRI models contributed equally to the MCS score.

INSERT TABLE 4 ABOUT HERE

Analyses of the effects of interactions between independent variables (group membership and EF variables) on the HRQOL dependent variables failed to reveal any significant interactions (all $ps > .074$; data not shown).

Discussion

The present study aimed to extend prior findings about HRQOL in a sample of stable, long-term adult survivors of PBT, by examining the potential influence of cognitive variables. We focused on the association between objective/reported EFs and HRQOL. We also wanted to identify the EFs that contributed most to HRQOL. Data of matched healthy controls were

included, as previous reports had demonstrated the contribution of EFs to HRQOL in nonclinical populations (e.g., Davis et al., 2010; Gamage et al., 2018; Huang et al., 2020).

First, preliminary analyses indicated that a subjective assessment of EFs addressing individuals' everyday experience is more sensitive than objective tasks when it comes to highlighting the late effects of PBT on executive functioning. Whereas the objective EF assessment only highlighted a deficit in one variable (working memory), self- and informant reports revealed several EF deficits. BRIEF-A GEC was impaired in both patients' and caregivers' reports, and patients and caregivers reported both metacognitive difficulties (MCI) and behavioral regulation deficits (BRI) (see Cantisano et al., 2021, for a more detailed analysis). This result helps to demonstrate the negative impact of EF sequelae on patients' everyday life, confirming recent data in patients with PBT (Loughan et al., 2020; van der Linden et al., 2020), and points to the importance of not relying solely on objective EF tasks to assess the late cognitive effects of PBT (see also Gehring et al., 2015).

In addition, intergroup comparisons showed that even several years after the end of treatment, HRQOL remained negatively impacted in patients with PBT. As perceived by patients and caregivers, this impact concerned both the physical and mental components of HRQOL. Up to now, it has mostly been observed in children or in adult survivors of brain tumors treated during childhood (e.g., Schulte et al., 2017). Data are scarce concerning long-term survivors of PBT diagnosed during adulthood (Boele et al., 2015; Giovagnoli et al., 1999; Solanki et al., 2017). Our result confirms that HRQOL should be assessed not only as a routine part of the clinical assessment during the treatment phase, but also in the long-term follow-up of survivors of PBT (Fernández-Méndez et al., 2019).

To meet our second and third objectives, we analysed the effect of executive functioning on HRQOL, while controlling for the effect of the group. Results revealed only a small effect of objective EF on HRQOL components, with a single variable (total number of errors on

MCST) associated with self-reported PCS. For their part, Davis et al. (2010) reported relationships between scores on two objective EF tasks (set-shifting and working memory) and a measure of HRQOL. By contrast, we found numerous relationships between reported EFs and HRQOL. For both self- and informant-reported measures, behavioral (BRI) and metacognitive (MCI) variables had a significant effect on both physical (PCS) and mental (MCS) components of HRQOL. All coefficients were significant and negative, indicating that greater executive capacities in everyday functioning are linked to better HRQOL.

More precisely, our findings showed that the physical component of HRQOL, which refers to perceived health, physical activities, and limitations in daily activities due to physical activity, was better explained by metacognitive variables (MCI index), including initiation, working memory, planning/organisation, and task monitoring. This finding indicates that EF processes associated with the regulation of activities make a major contribution to the corresponding HRQOL components, in line with previous studies suggesting that changes in EFs correspond to changes in physical activity, in both children (Gottwald et al., 2016) and adults (Corti et al., 2017). Interestingly, this relationship may be bidirectional, for just as low levels of physical activity may lead to a decline in EFs, so a lower level of executive functioning may also be associated with a reduction in physical activity (Daly et al., 2015).

By contrast, EF behavioral processes (BRI), including inhibition, emotion control, and self-monitoring, contributed most to the mental component of HRQOL (above all self-reported, but also informant-reported), which includes variables such as life/relationships with others. This finding confirms the crucial contribution of executive processes associated with self-/emotional regulation to HRQOL components related to social activities. Previous research has highlighted relationships between social outcomes and executive functioning in various etiologies (e.g., Campbell et al., 2009; Penadés et al., 2010), as well as in healthy populations (e.g., Jacobson et al., 2011; Riggs et al., 2006). In neuro-oncology, such research is scarce, but

one recent study confirmed the link between reported EFs and social skills in survivors of pediatric PBT (Desjardins et al., 2020).

Remarkably, we found no interaction effect between the independent variables (group membership, executive variables), which means that there were no differences between groups regarding the effect of EFs on HRQOL, even though patients had deficits on these variables. The associations between self-reported executive functioning and both physical and mental HRQOL components confirm the conclusions of previous studies. Prior findings had demonstrated an association between wellbeing and scores on questionnaires assessing cognitive functioning in patients with glioma (Gehring et al., 2015). In pediatric patients with PBT, a relationship has been highlighted between reported EFs and HRQOL (Netson et al., 2016; Ventura et al., 2018). In other populations of cancer survivors, self-reported EFs have been found to be more predictive of functional impairments than objective EF measures among survivors of breast cancer (Calvio et al., 2010). In healthy individuals, relationships between EFs and HRQOL have previously been demonstrated using a self-reported scale (Huang et al., 2020), but there have been very few studies on this topic. Our study therefore helps to confirm that the influence of EFs on HRQOL concerns both clinical and nonclinical populations, in accordance with the theoretical tenets of executive functioning (e.g., Lehto, 1996; Miyake et al., 2000).

Clinical implications

From a clinical point of view, given that there were numerous differences on reported EFs and HRQOL between patients and controls in our study, findings suggest that executive limitations negatively impact different facets of HRQOL among long-term, stable adult survivors of PBT. Executive functioning is generally assumed to impact HRQOL by influencing patients' ability to plan/organise behavior, monitor their actions, and remember things they have to do in the short term. In the present study, we provide more specific evidence

about the executive components that may influence both the physical and mental components of HRQOL. To the best of our knowledge, this is a novel and original contribution to the field, as most reports demonstrating relationships between cognition and HRQOL have used tasks that do not necessarily reflect the difficulties encountered by patients in everyday life. Given that improving HRQOL is one of the major objectives in survivorship care, our study helps to demonstrate that EF interventions designed to remediate behavioral difficulties could be particularly useful for enhancing HRQOL in adult survivors of PBT. Although the cognitive rehabilitation of patients with PBT is still in its infancy, it has already yielded promising results (Bergo et al., 2016; Loughan et al., 2019). EF interventions, which can include cognitive rehabilitation (Richard et al., 2019) and virtual reality environments (Yang et al., 2014), could be particularly useful for promoting HRQOL in adult PBT survivors.

Limitations

The present study had several limitations. First, while this is not specific to our sample, the patient group was heterogeneous in terms of treatments and tumor type/grade. Nevertheless, comparisons between patient subgroups according to etiology did not reveal any differences on any of the variables in our study. A more detailed analysis was beyond the scope of this work, given the small sample size. As some authors have reported a continuing and substantial decline in HRQOL several years after treatment end, regardless of tumor type (Zamanipoor Najafabadi et al., 2017), the present study was designed to explore the influence of EF limitations on the HRQOL of adult survivors of PBT, regardless of etiology. In addition, some research has shown that chemotherapy and radiotherapy have similar effects on cognitive functioning and HRQOL in patients with PBT, and the addition of chemotherapy to radiotherapy has no influence on these variables (Reijneveld et al., 2016). Second, a more comprehensive assessment of language, attention and memory skills could have been conducted, as these abilities have been shown to be related to executive functioning (e.g., Baudic et al., 2006; Fellows et al., 2014;

Velichkovsky et al., 2019). Third, as EFs are known to be closely associated with everyday outcomes, it would be interesting to add measures of daily-life activities or occupational rehabilitation indicators in future studies, in addition to measures of reported EFs. Fourth, self-report cognitive assessments may be impacted by psychological distress (e.g., Nicol et al., 2019). Therefore, another important limitation of this study is that we did not assess psychological distress.

Conclusion

Despite its preliminary nature, and from a clinical point of view, this study demonstrates that even several years after end of treatment, adult survivors of PBT may experience daily-life behavioral disorders induced by executive impairments that negatively influence their HRQOL. In neuro-oncology, patients' reported outcomes are now assumed to guide clinical practice, by providing information about late cancer effects (Molinari et al., 2019). A biopsychosocial model of survivorship care has been developed, with a list of outcomes to consider (including cognitive status and HRQOL), to bring together patients' representations of disease sequelae (Leeper & Milbury, 2018). By reporting these representations and demonstrating the contribution of reported EF changes to HRQOL, our study is fully in line with this perspective.

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Disclosure of interest

The authors have no conflict of interest to declare.

Ethics approval

The present study received French regulatory ethical approval (Comité de Protection des Personnes Ouest II, no. 2015/27, ID-RCB no. 2015-A01192-47) which includes the International Review Board Authorisation (No. NCT02693405). The Angers University Hospital was the study's promoter.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent for publication

Participants signed informed consent regarding publishing their data.

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Table 1. Participants' sociodemographic characteristics and patients' medical information.

Characteristics	Patients with PBT (n = 40)	Controls (n = 40)
	Mean (\pm SD) / Number (%)	Mean (\pm SD) / Number (%)
Age in years, range	41.20 (11.06), 18-59	40.88, (11.06), 18-59
Sex		
Men	28 (70%)	25 (63%)
Women	12 (30%)	15 (37%)
Handedness		
Left handed	5 (12.5%)	2 (5%)
Right handed	34 (85%)	36 (90%)
Ambidextrous	1 (2.5%)	2 (5%)
Education in years ^a	11.83 (3.29)	12.38 (2.87)
Years since end of treatment	3.67 (2.31)	--
Informant ^b		
Spouse	30 (81.1%)	18 (69.2%)
Close family member	7 (18.9%)	8 (30.8%)
Tumor type		
Oligodendroglioma	11 (27.5%)	--
Oligoastrocytoma	5 (12.5%)	--
Subependymoma	1 (2.5%)	--
Astrocytoma	6 (15%)	--
Glioblastoma	3 (7.5%)	--
Radiologically diagnosed glioma	5 (12.5%)	--
Ganglioglioma	2 (5%)	--
Other tumors ^c	7 (17.5%)	--
Grade		
Low-grade glioma	18 (45%)	--
High-grade glioma	15 (37.5%)	--
Non-glioma tumor ^c	7 (17.5%)	--
Tumor site		
Frontal/ Frontotemporal	23 (57.5%)	-
Other	17 (42.5%)	-
Treatments		
Tumor resection	15 (37.5%)	-
Chemotherapy and radiotherapy	1 (2.5%)	-
Chemotherapy and tumor resection	5 (12.5%)	-
Radiotherapy and tumor resection	5 (12.5%)	-
Chemotherapy and radiotherapy and tumor resection	14 (37.5%)	-
Epileptic seizures		
No	37 (92.5%)	-
Yes	3 (7.5%)	-

Note. ^a Number of years education after first grade (elementary school); ^b Some informant-reported data were lost, especially in the control group (several participants' proxies did not return their questionnaires); ^c craniopharyngioma, meningioma, medulloblastoma, neurocytoma, germinoma.

Table 2. Mean comparisons between patients with PBT and healthy controls on sociodemographic characteristics, executive variables (objective and behavioral), and HRQOL reports.

	Patient Group Mean (SD)	Control Group Mean (SD)	<i>t</i>	<i>df</i>	<i>p</i>	<i>d</i>
MMSE	27.91 (2.18)	28.58 (1.81)	-1.41	69	.16	0.33
Objective EF measures						
Stroop (total number of errors)	0.52 (2.11)	0.13 (0.89)	1.08	77	.28	0.24
Digit Span Forward	8.67 (2.47)	9.42 (2.31)	-1.40	78	.16	0.44
Digit Span Backward	8.90 (2.66)	10.25 (2.77)	-2.22	78	.03	0.33
MCST (total errors)	6.70 (7.57)	5.48 (4.60)	0.88	78	.38	0.20
Behavioral EF measures (BRIEF-A)						
<i>Self-reported</i>						
BRI	52.28 (12.78)	47.63(8.85)	1.89	78	.07	0.42
MCI	53.20 (12.17)	47.90 (9.21)	2.20	78	.03	0.49
GEC	53.13 (12.10)	47.28 (9.10)	2.44	78	.02	0.54
<i>Informant-reported</i>						
BRI	48.73 (8.84) ^a	44.10 (8.09) ^b	2.23	66	.03	0.55
MCI	50.27 (9.77) ^a	45.65 (9.90) ^b	1.93	66	.06	0.47
GEC	49.22 (9.73) ^a	44.29 (9.22) ^b	2.12	66	.03	0.52
			<i>F</i>	<i>df1, df2</i>	<i>p</i>	<i>η²</i>
HRQOL (SF-36)						
<i>Self-reported</i>						
PCS	28.92 (1.11)	29.41 (0.90)	5.147	1,74	.03	.058
MCS	23.09 (1.41)	23.8 (1.37)	5.935	1,74	.02	.06
<i>Informant-reported</i>						
PCS	28.95 (1.17) ^a	29.53 (0.85) ^b	5.262	1,58	.03	.075
MCS	23.12 (1.13) ^a	24.17 (1.01) ^b	16.617	1,58	<.001	.191

Note. ^a *n* = 37; ^b *n* = 31; *SD* = standard deviation; MCST = Modified Card Sorting Test; BRI = Behavioral Regulation Index; MCI = Metacognition Index; GEC = Global Executive Composite; PCS = physical component score; MCS = mental component score. Significant values are in bold.

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Table 3. ANCOVA models showing beta coefficients, η^2 and BIC values between executive factors and components of HRQOL for self-reported measures.

Executive factor (BRIEF-A)	HRQOL component (SF-36)	
	PCS	MCS
BRI		
Beta	-0.34**	-0.44***
η^2	.113	.186
BIC	228.9	270.9
MCI		
Beta	-0.36**	-0.35**
η^2	.127	.117
BIC	227.6	277.7

Note. * $p < .05$. ** $p < .01$. *** $p < .001$. BRI = Behavioral Regulation Index; MCI = Metacognition Index; PCS = physical component score; MCS = mental component score.

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Table 4. ANCOVA models showing beta coefficients, η^2 and BIC values between executive factors and components of HRQOL for informant-reported measures.

Executive factor (BRIEF-A)	HRQOL component (SF-36)	
	PCS	MCS
BRI		
Beta	-0.29*	-0.38***
η^2	.08	.143
BIC	189.1	187.8
MCI		
Beta	-0.44***	-0.39***
η^2	.195	.150
BIC	180.1	187.2

Note. * $p < .05$. ** $p < .01$. *** $p < .001$. BRI = Behavioral Regulation Index; MCI = Metacognition Index; PCS = physical component score; MCS = mental component score.

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