Screening for cognitive deficit in 8 to 14 year old children with cerebellar tumors using self-report measures of executive and behavioral functioning and health-related quality of life

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Running head: IQ screening in children with cerebellar tumors

Abstract

Background We aimed to identify a brief screening measure for detection of cognitive deficit in children treated for cerebellar tumors that would be useful in clinical practice.

Methods A sample of 72 children aged 8-14 years and within three years post-diagnosis for standard risk medulloblastoma (n=37) or low grade cerebellar astrocytoma (n=35) and 38 in a non-tumor group were assessed using teacher-, parent-, and child-report of the Behavior Rating Inventory of Executive Function (BRIEF), Strengths and Difficulties Questionnaire (SDQ), and Pediatric Quality of Life Inventory (PedsQL). The accuracy of these scores as a screen for a full scale Intelligence Quotient (FSIQ) <80 on the Wechsler Intelligence Scale for Children (WISC®-IV UK) was assessed using their receiver operating characteristic (ROC) curves.

Results The questionnaires with the highest areas under the ROC curves were the child- and parent-report PedsQL and the teacher-report BRIEF and SDQ. At optimal cut-off scores, their sensitivities (95% CIs) to cases of FSIQ<80 were 84 (60-96)%, 65 (41-84)%, 79 (54-93)%, and 84 (60-96)% and their specificities (95% CIs) were 79 (68-86)%, 87 (77-93)%, 77 (66-86)%, and 71 (64-84)% respectively. All cases of FSIQ<80 screened positive on either teacher-report SDQ or self-report PedsQL.

Conclusions The PedsQL child- and parent-report and the teacher-report BRIEF and SDQ have moderately good accuracy to discriminate between children with and without a FSIQ<80. The PedsQL could be used in a clinical setting, and the BRIEF and SDQ in an educational setting, to screen for cases with FSIQ<80 in children treated for brain tumors.

Key words screening; cognitive deficit; children; cerebellar tumors; health-related quality of life

Introduction

Brain tumors are second in incidence to leukemia among neoplasms of childhood and constitute 23% of all tumors that develop before the age of 15.[1] Actuarial 5-year survival for all CNS tumors combined was 72-75% among those diagnosed in the UK during 2001-2010[2] and 72% (95% CI 71-73%) in the SEER-18 cancer registries in the USA during 1995-2010.[3]

About half of long-term survivors of childhood brain tumors experience significant neurocognitive impairment[4,5] attributed to the tumor itself, hydrocephalus, neurosurgery,[6] adjuvant radiotherapy,[7] or radiotherapy and chemotherapy in combination.[8] They achieve significantly lower educational attainment than the general population[9] and suffer long term socio-economic and work place disadvantage.[10,11] There is international agreement among experts that cognitive and psychosocial deficits affect health-related quality of life (HRQoL) among child and adolescent survivors of cancer and monitoring of them should be a priority.[12] To address these issues, there is a need for early and continuing systematic assessment of these children to identify the need to expedite the implementation of clinical psychology and other services that would enable timely rehabilitation[9,13-15] to improve their life chances.

However, systematic assessment is not always achieved in practice,[9,13,16,17] even though guidelines advocate such access for all families,[17,18] due to limited access to Clinical Psychology services that might provide this service.[16,17] Prior attempts to screen specifically for cognitive deficits have used direct assessments requiring face-to-face administration[19-22] which is resource intensive. They typically need to be executed by a trained assessor[19,20] or psychologist[21,22] in a designated quiet room in a hospital setting and the additional time needed may prolong the hospital visit for the patient by up to 75 minutes.[21] Alternatively screening for cognitive deficit using brief, accurate, psychometrically robust self-report measures in a clinical setting, without

initially the need to engage psychological services might achieve this where limited resources preclude face-to-face psychometric assessments. Those falling above or below specified cut off scores indicating clinical risk could then undergo a full rehabilitation assessment and be considered for intervention. Self-report paper and pencil measures have been successfully applied in clinical settings to screen for psychosocial difficulties in children treated for cancer[23-27] and a measure of parent-perceived cognitive function showed good ability to discriminate between childhood cancer survivors with and without a brain tumor.[28]

We found that cognition and emotion accounted for more than half of the variance in HRQoL scores in a representative sample of children treated for cerebellar tumors in the UK[15] and many other studies have found cognitive function to be associated with HRQoL.[29-31] Our observations[15] led us to hypothesize that poor scores on self-report measures of HRQoL, executive function, and behavioral function might be sufficiently accurate to be usable not only as a screen for deficits in those domains but also as screening tests for the presence of deficits in full scale intelligence quotient (FSIQ) in these children. We therefore examine here the accuracy of three widely available questionnaire measures with good psychometric properties as screens for the detection of children with borderline or greater cognitive deficit, defined as a FSIQ<80.[32] As far as we are aware, this is the first time that the accuracy of self-report measures as screening tests for detection of cognitive deficit, as defined by direct psychometric assessment, in children with cerebellar tumors.

Materials and Methods

Design

The present study was part of a multi-center prospective longitudinal HRQoL study that was undertaken from February 2005 to January 2010.

Patients

We have previously reported the population studied and methods used to obtain both questionnaire responses and FSIQ assessments from them in our report on factors predicting their HRQoL two years after enrolment in the study.[15] Briefly, the participants were children aged 8-14 years with either 'standard risk' medulloblastoma (i.e. less than 1.5 cm^3 residual tumor and no evidence of metastatic disease) or low grade cerebellar astrocytoma diagnosed within the preceding three years. They were recruited from 11 of the 20 Children's Cancer and Leukaemia Group (CCLG) Children's Cancer Treatment Centres (CCTCs) in England and Wales over a period of 20 months. A non-tumor comparison group was randomly selected from the same year groups of the schools attended by children in the tumor groups. The only non-inclusion criteria in each group were premorbid disability or inability to communicate in the English language but these criteria were not met in any child referred to the study. For the present study of the accuracy of questionnaires as screens for concurrent deficits in FSIQ, non-availability of a FSIQ score at enrolment to the study was an exclusion criterion that was applied to six of the 110 participants in the HRQoL study.

All participating children diagnosed with cerebellar tumor had undergone neurosurgical removal of the tumor. Those with medulloblastoma also received adjuvant treatment comprising six weeks of daily craniospinal radiotherapy of 23.4 Gy with a boost to 55.8 Gy to the posterior fossa and 'Packer' regimen chemotherapy (weekly vincristine for eight weeks followed six weeks later by eight, six week cycles of chemotherapy consisting of CCNU and cisplatin plus vincristine, given weekly for three weeks).[33] There were no major deviations from this standard treatment.

Measures

We selected the following measures for their good psychometric properties, brevity, and applicability to children with brain tumors:[15,22,37-39] parent- and teacher-report of the child's executive function in everyday life using the Behavior Rating Inventory of Executive Function (BRIEF);[34] parent-, teacher- and child-report of the child's behavior using the Strengths and Difficulties Questionnaire (SDQ);[35] and parent- and child-report of the child's HRQoL using the Pediatric Quality of Life Inventory (PedsQL).[36] [15,22,37-39]Additionally these seven questionnaires are of relatively low cost and widely used in departments of Clinical Psychology. The Wechsler Intelligence Scale for Children®-4th UK Edition (WISC®-IV UK)[32] was administered as a 'gold standard' measure of cognitive function. We chose a FSIQ score <80 as the defining threshold below which participants were classified as having borderline or greater cognitive deficit, according to the WISC®-IV UK manual.[32] In a typically developing population, 9% of children and young people would be expected to be 'cases' (i.e. produce a FSIQ score <80) because this is the percentage of a normal distribution expected to fall more than 1.33 SD below the population mean and has been used in previous descriptions of cognitive deficits in similar populations.[40,41] In our sample of children treated for cerebellar tumors, this degree of deficit was present in 19/66 (29%) children and identifying them would therefore be a way of identifying that proportion of the population in whom cognitive evaluation was most likely to lead to interventions to support learning.

Procedure

Children fulfilling inclusion criteria were identified from hospital discharge and clinic lists and referred to the study center by the treating clinicians. Written informed consent was obtained from all participating parents and children. Assessments were undertaken in the family home to which questionnaires were sent by post in advance while the WISC was administered at the visit

itself. Parents provided information on pre-morbid socio-economic status (SES) classified according to the UK Office for National Statistics Socio-economic Classification (ONS 2004). Teacher questionnaires were mailed to schools following the home visit. The protocol for this study was approved by the UK CCLG. Ethical approval was obtained from the Trent Multi-Centre Research Ethics Committee, UK.

Statistical analyses

All available FSIQ scores, assessed at enrollment into the study, were included in the analyses. Screening accuracy was evaluated by plotting receiver operating characteristic (ROC) curves for each measure. The ROC curve is an X-Y graph of the accuracy of a screening test for a target condition. Sensitivities at all possible screening test threshold scores are plotted on the Y-axis against 1–specificity on the X-axis. A 45^{o} diagonal line indicates a screening test operating at a chance level of separating true positive from true negative cases of the target condition. Youden's index, the maximum orthogonal distance between the 45^{o} diagonal line and the ROC curve, identifies the optimal cut-off score that maximizes the extent to which the test separates true positives from true negatives.[42] The area under the ROC curve (AUC) gives an overall summary of the accuracy of the screening test in identifying the target condition: AUCs of >0.90, 0.70 to 0.90, and 0.50 to 0.70 are commonly taken to indicate high, moderate, and low accuracy respectively while an AUC of 0.50 indicates a chance result.[42] Having identified the optimal screen threshold score using Youden's index, the sensitivity (proportion of true positives that screen positive), specificity (proportion of true negatives that screen negative), likelihood ratio for a screen positive (LR+, the ratio of the probability of a true positive to the probability of a false positive) and for a screen negative (LR-, the ratio of the probability of a false negative to the probability of a true negative) for that threshold score were calculated for the total sample. A

LR+ >7.00 and a LR- <0.30 indicate high screening accuracy.[43] Youden's index, the AUC, sensitivity, specificity, LR+, and LR- are independent of the prevalence of a condition whereas positive and negative predictive values are not.[43] The AUCs, sensitivities and specificities were calculated and their 95% confidence intervals used to define the precision of the estimates of the accuracy of the screening tests. All analyses were conducted using IBM SPSS version 21.

Results

Sample characteristics

Seventy-six children treated for cerebellar tumors were referred to the study center. Of these, 72 (95%), comprising 37 with medulloblastoma and 35 with astrocytoma, were enrolled over a 20 month period of which FSIQ data obtained at the first assessment were available in 32 and 34 children in the respective groups. The annual rate of enrolment into the study over the 1.8-year recruitment period was 104% for medulloblastoma and 87% for astrocytoma of the expected number of diagnoses of eligible cases at participating centers over that time, estimated from the relevant figures for disease incidence and time trends in the UK population.[15] Of the 38 participants in the non-tumor group, 25 were the first random choice, and seven were the second random choice, the first family having declined to participate. FSIQ data obtained at the first assessment were available in all of these. In the present study the 66 children treated for cerebellar tumors had a mean (range) time interval from tumor diagnosis of 16.3 (1-35) months (Table 1). Child and parent demographic characteristics were similar in the two tumor groups and the non-tumor group at recruitment excepting an excess of lone parents, only children, lower parental educational qualifications, and occupations other than managerial or professional in families of children treated for medulloblastoma (Table 1). Mean scores for each measure showed poorer functioning in the tumor groups compared with the non-tumor group (Table 2).

Screening accuracy of each measure

Thirteen (41%) of those with medulloblastoma and 6 (18%) of those with cerebellar astrocytoma had a FSIQ<80, compared to 1 (3%) in the non-tumor group (Tables 3 and Appendix Table e1). Among the 18 children treated for cerebellar tumours that had FSIQ<80, and for whom we had information about special education services, 3 (17%) were not attending school regularly, 3 (17%) were receiving no extra help, 5 (28%) were receiving help commensurate with their class mates, typically with reading and mathematics, and 7 (39%) were receiving specific individual help. Evaluation of the suitability of all seven questionnaires as a screen for FSIQ<80 demonstrated that they performed significantly better than chance to detect that condition (p<.001) and with moderate accuracy, indicated by AUCs that ranged between 0.73 and 0.85 (sensitivities ranging from 0.55 to 0.84, specificities ranging from 0.71 to 0.87; and LR+ values ranging from 2.74 to 4.90) (Table 4). The 95% CI of four of the seven questionnaires fell entirely within the high to moderate accuracy range. These were the child- and parent-report PedsQL and the teacher-report BRIEF and SDQ (Table 4).

Youden's index identified the optimum screen threshold score. Child-report PedsQL had the greatest AUC (score <65=positive screen, sensitivity 0.84, specificity 0.79, and LR+ of 3.93). Parent-report PedsQL (score <51=positive screen, sensitivity 0.65, specificity 0.87, LR+ 4.90), teacher-report BRIEF (score >59=positive screen, sensitivity 0.79, specificity 0.77, LR+ 3.46), and SDQ (score >7=positive screen, sensitivity 0.84, specificity 0.71) had AUCs that were slightly lower but with 95% CIs that overlapped with that of the AUC for child-report PedsQL (Figure 1; Table 4).

Screening by using a score beyond the threshold value on either the teacher-report SDQ (sensitivity 0.84, specificity 0.71) or the self-report PedsQL (sensitivity 0.84, specificity 0.79)

increased sensitivity (95% CI) to cases of FSIQ<80 to 1.00 (0.79-1.00) (Appendix Table e1) but reduced specificity (95% CI) from the above figures to 0.65 (0.53-0.75) (figures not tabulated).

Discussion

All screening measures correctly identified 55-84% of children with borderline or greater deficit in FSIQ and correctly identified 71-87% of children without a deficit. The precision of these estimates was sufficient to indicate that the child- and parent-report PedsQL and the teacher-report BRIEF and SDQ were moderately or highly accurate screens. Screening positive on any one of the child-report PedsQL or the teacher-report SDQ correctly identified all cases with FSIQ<80 but decreased the specificity of the screen.

Our findings are likely to be generalizable to the great majority of children with cerebellar tumors for two reasons. First, we included the two most common tumor types and the two most common combinations of treatment modalities, namely surgery alone and surgery combined with both cranio-spinal radiation therapy and chemotherapy. Second, the population base, comprised of the catchment area populations of half (11 of 22) of all UK CCTCs, was large and the number of children in the tumor groups that were enrolled was close to the total number of cases predicted, from UK national figures for incidence and time trends, to present over the 20 month recruitment period.[44]

The inclusion of an unbiased sample of children of the same age in the general population but without tumors enabled us to increase the sample size and therefore the precision of our estimates of accuracy as indicated by likelihood ratios and similar measures of accuracy that are independent of the population prevalence of the target condition unlike predictive values which are prevalence dependent.[43,45]

The use of the WISC as a gold standard measure of cognitive function is a strength of this

study and the choice of threshold of FSIQ<80, below which 9% of a typically developing population and 29% of our sample of children treated for cerebellar tumors falls, is a reasonable pragmatic decision, especially when resources only allow direct assessment of a minority of cases.

The added benefit of the three questionnaires that we used is that they also provide a screen for problems with executive function, behavioral and emotional problems, and HRQoL and their constituent domains of functioning which is another strength of the approach described in the present study as it thus avoids focusing too narrowly on those who display low IQ. In fact two of these three measures are included in the short battery of assessments devised and shown to be deliverable in the setting of a USA Children's Oncology Group trial.[22] The PedsQL has been shown to have an impact on clinical intervention decision making in pediatric clinic settings for children with rheumatology, cardiology, and orthopedic problems.[27] An et al. (2013)[29] reported strong correlations between child-report PedsQL and FSIQ in children aged between 6 and 13 years treated for brain tumors. This is supported by the present study.

Conversely, one potential limitation of a screening approach is its reduction of cognitive ability to any single number and the accompanying narrowing of the scope of the cognitive deficits to which it is sensitive. This is to some extent unavoidable in the quest for a simple short screening test which requires definition of a unitary 'target condition'. Many survivors of CNS tumors have problems with specific skills like attention and processing speed that will significantly impair their academic performance without leading to a decrease in their FSIQ to less than 80[8] and, if access to a clinical psychologist can be obtained routinely, a full psychological evaluation, including tests of attention, processing speed, working memory, and executive function[4,7,8,46,47] is preferable to any single screening test. When, on the other hand, it

is not possible for the child to gain access to a psychometric assessment, some cases in which there are specific cognitive deficits in which the BRIEF score was not sufficiently abnormal to constitute a positive screen for FSIQ<80, would nevertheless come to light by closer examination of BRIEF scores and sub-scores by a psychologist who has the knowledge and training to interpret BRIEF profiles. For these reasons, the screening approach that we propose does not oversimplify problems into a binary 'Yes/No' decision separated by a dividing line at FSIQ=80 but permits consideration of the executive, emotional, physical and psychosocial aspects that impinge on cognitive function. Examination of subscale scores might be seen as defeating the purpose of screening that needs to divide those screened into screen positive and screen negative groups but future work could examine the incorporation into the screening process of simple reports, based on automated on-line scoring, in which subscale scores that identify neurocognitive dysfunction evident before FSIQ scores are affected (e.g., processing speed, working memory) could be categorized by scoring centile as green, amber, or red.

A second limitation of our study, designed primarily to assess HRQoL in children old enough to provide reliable self-report and young enough to remain within the pediatric age range after 24 months of follow-up, was the fact that the age range was restricted to 8 to 14 years. Our findings may not apply to younger children although children as young as 5 years can reliably and validly self-report using the PedsQL.[48] Further studies are also needed in children treated for tumors in other, particularly supratentorial, locations to examine the performance of these screening measures in those contexts.

Teacher-report of executive function and behavioral difficulties proved to be an accurate source of information about a child's cognitive and behavioral functioning in our study and was relatively strongest in those treated for medulloblastoma, in whom it correctly identified 85-92%

of true cases of FSIQ<80 compared to only 60% of true cases in the astrocytoma group. In contrast, parent- and child-report HRQoL correctly identified 83-100% of true cases in the astrocytoma group but only 67-75% of cases in the medulloblastoma group. This may indicate differences in the variation in screening accuracy of the measures within a clinical context or in the sensitivity of teacher-, child-, and parent-report to cognitive deficits or in both. This could be explored in future research in a larger sample of children treated for low-grade astrocytoma as this group contained few cases of FSIQ<80 in the present study.

Our finding that accuracy of 100% was obtainable by accepting a score beyond the threshold value for either the self-report PedsQL or the teacher-report SDQ was adopted as a strategy *post hoc* and in future research this needs to be tested in an independent sample. If high accuracy were confirmed, the use of teacher-reports as an approach to screening would only succeed in an educational context in which teachers are willing to provide their responses to health providers. Such success in liaising with teachers would itself constitute an important step towards aligning clinical and educational perspectives on the child's needs.

It is important to stress that we would recommend repeated annual screening through the acute phase of survival into the longer-term during the school years for the detection of cognitive deficits as problems emerge over time.[29,41] Participants in the present study were all less than three years from diagnosis at enrolment and both tumor groups in fact showed an increase in their group mean FSIQ over the 24 months for which they remained in the study[15] but it is well established that a failure to acquire new skills may lead to a fall in FSIQ over time in children treated with cranial radiotherapy[8] as well as those treated with neurosurgery alone,[46] with some problems not fully manifested until more than 5 years from diagnosis.[4] It is possible that the screening battery used here may be sensitive to neuropsychological difficulties related to medical

factors known to affect cognitive processes more acutely in the peri-operative period (e.g. complications of treatment of hydrocephalus, peri-operative infections or hemorrhage) rather than those that emerge over time. Nonetheless, 85% of the sample had been diagnosed more than six months previously and were therefore well out of the peri-operative period.

In clinical settings where access to pediatric neuropsychologists is readily available, we support the use of a short battery such as those proposed by Embry et al.[22] in the USA or by Ottensmeier et al. (2014)[49] in Germany and have made recommendations, together with colleagues from 10 other countries across Europe, on the domains and assessments of those domains that should be prioritized for assessing survivors of childhood brain tumors.[39] These psychometric assessments are, however, often not available outside Europe and North America or in some countries within Europe, even in the context of treatment trials and are not undertaken in most children treated in any country outside the setting of a clinical trial (e.g. many children with low grade cerebellar astrocytomas). By contrast, the application of questionnaires has been achieved across several European countries in a treatment trial for medulloblastoma,[37] is being achieved with web-based versions of the questionnaires in a European treatment trial currently and is potentially applicable over a wider geographical area and clinical context. The present study suggests that where access to psychometric assessment is limited, questionnaires may also provide a pragmatic screen to prioritize direct psychometric assessment of those most likely to have cognitive deficits in FSIQ and therefore very likely to be in need of support to ameliorate these difficulties.

The fact that only 39% of the children treated for cerebellar tumours that had a FSIQ<80 had been identified as having specific educational needs at school, reflects the lack of experience of schools in meeting the needs of the relatively rare child with newly acquired, rather than

developmental, cognitive deficits and suggests that screening of children for low FSIQ by those delivering their health care could help to alert schools to the need for assessment for individual special educational needs. These survivors may actually be most in need of neuropsychological follow-up in order to characterize their developing pattern of difficulties, and to initiate treatment or services before the problems worsen and cause greater functional impairment. The extent to which this applies to countries other than the UK merits further study.

In summary the child- and parent-report PedsQL and the teacher-report BRIEF and SDQ have moderately good discriminative power to differentiate children with and without a FSIQ<80 including 79-84% sensitivity to FSIQ<80. The PedsQL could be used in a clinical setting and the BRIEF and SDQ in an educational setting to detect cognitive deficits as well as problems with emotional and behavioral disorders, executive dysfunction and poor HRQoL in children treated for a brain tumor and indicate the need for referral for a fuller psychological evaluation from an early stage.

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Figure Legend

Figure 1

ROC curves showing percentages of sensitivity and specificity for the three measures that show the highest accuracy in detecting a FSIQ<80

PedsQL (n=103), Pediatric Quality of Life Inventory;[36] BRIEF (n=98), Behavior Rating Inventory of Executive Functioning;[34] SDQ (n=99), Strengths and Difficulties Questionnaire.[35]

Table

Table 1. Child and parent characteristics by tumor group

		Medulloblastoma n=32	Astrocytoma n=34	Non-tumor n=38
Mean age in years (range)		10.2 (8-14)	10.4 (8-14)	10.4 (8-14)
Mean age in years at diagnosis (range)		8.8 (6-13)	9.2 (5-14)	N/A
Mean months from diagnosis (range)		17.6 (1-35)	15.0 (1-35)	N/A
Parent mean age in years (SD)		38.7 (5.1)	40.8 (8.2)	40.5 (5.3)
		n (%)	**n (%)**	**n (%)**
Female		13 (41)	23 (68)	19 (50)
Mother respondent		31 (97)	31 (91)	33 (87)
Lone parent family		6 (19)	3 (9)	5 (13)
Only child		6 (19)	3 (9)	4 (11)
Parent education:	None	1 (3)	2 (6)	2 (5)
	School	12 (38)	5 (15)	7 (18)
	College	14 (44)	18 (53)	21 (55)
	University	4 (13)	9 (27)	8 (21)
	Unknown	1 (3)	0	0
SES pre-diagnosis:	Managerial/Professional	9 (28)	21 (62)	18 (47)
	Intermediate	12 (38)	8 (24)	7 (18)
	Routine & Manual	7 (22)	5 (15)	10 (26)
	Not working	3 (9)	0	3 (8)
	Unknown	1 (3)	0	0

N/A, not applicable; SD, standard deviation; SES, socio-economic status.

Table

Table 2. Mean (SD) scores for each screening measure by tumor group

Measure	Medulloblastoma n=32*	Astrocytoma n=34*	Non-tumor n=38*
†BRIEF (*T* score mean=50, SD=10)			
Parent	55.3 (12.5)	56.3 (11.4)	51.2 (10.0)
Teacher	60.1 (13.2)	56.9 (14.4)	51.0 (9.0)
†SDQ (possible range 0-40)			
Parent	10.7 (6.7)	10.0 (6.0)	8.1 (5.3)
Child	9.7 (4.8)	10.0 (5.8)	8.8 (5.5)
Teacher	9.0 (5.2)	6.2 (5.1)	4.7 (5.0)
‡PedsQL (possible range 0-100)			
Parent	51.5 (20.8)	68.2 (23.9)	84.3 (11.0)
Child	61.2 (18.2)	71.3 (20.4)	82.1 (12.3)

BRIEF, Behavior Rating Inventory of Executive Functioning;[34] SDQ, Strengths and Difficulties Questionnaire;[35] PedsQL, Pediatric Quality of Life Inventory;[36] FSIQ, full scale IQ; SD, standard deviation

*: numbers varied slightly for each measure and informant; higher scores,

†: higher scores indicate increased dysfunction

‡: higher scores indicated better quality of life

Table

Table 3. Screening for cognitive deficit following medulloblastoma, low grade cerebellar astrocytoma and in a non-tumor comparison group: performance of three self- and proxy-report questionnaires.

				Target condition of WISC FSIQ<80 present (+) or absent (-)					
				Medulloblastoma		Astrocytoma		Non-tumor	
				+	-	+	-	+	-
				n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
FSIQ<80 n (%)				13 (41)	19 (59)	6 (18)	28 (82)	1 (3)	37 (97)
Screen positive (+) or screen negative (-) at optimal cut-off score point	**BRIEF**	Parent (>57)	+	8 (62)	4 (21)	6 (100)	10 (36)	1 (100)	7 (19)
			-	5 (38)	15 (79)	0	18 (64)	0	30 (81)
		Teacher (>59)	+	11 (85)	3‡ (19)	3* (60)	8* (30)	1 (100)	7* (19)
			-	2 (15)	13‡ (81)	2* (40)	19* (70)	0	29* (81)
	SDQ	Child (>11)	+	9* (75)	4 (21)	3 (50)	10 (36)	1 (100)	7 (19)
			-	3* (25)	15 (79)	3 (50)	18 (64)	0	30 (81)
		Parent (>14)	+	6 (46)	3 (16)	5 (83)	4 (14)	1 (100)	4 (11)
			-	7 (54)	16 (84)	1 (17)	24 (86)	0	33 (89)
		Teacher (>7)	+	12 (92)	6† (35)	3* (60)	8* (30)	1 (100)	6* (17)
			-	1 (8)	11† (65)	2* (40)	19* (70)	0	30* (83)
	PedsQL	Child (<65)	+	9* (75)	9 (47)	6 (100)	6 (21)	1 (100)	3 (8)
			-	3* (25)	10 (53)	0	22 (79)	0	34 (92)
		Parent (<51)	+	8 (62)	9* (50)	5 (83)	2 (7)	0	0
			-	5 (38)	9* (50)	1 (17)	26 (93)	1 (100)	37 (100)

BRIEF, Behavior Rating Inventory of Executive Functioning;[34] SDQ, Strengths and Difficulties Questionnaire;[35] PedsQL, Pediatric Quality of Life Inventory;[36] FSIQ, full scale IQ

*: 1 missing value

†: 2 missing values

‡: 3 missing values

Table

Table 4. Screening accuracy to detect a FSIQ<80 based on maximum Youden's Index for each measure

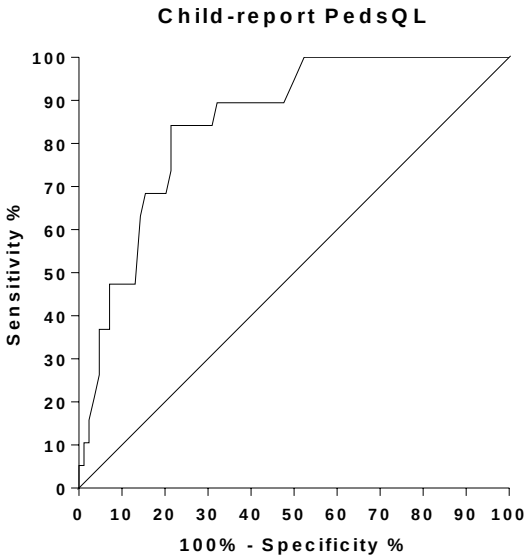
Measure	N	Informant	Cut-off score	AUC (95% CI)	Sens% (95% CI)	Spec% (95% CI)	LR+	LR-	J
BRIEF*	104	Parent	>57	.76 (.61 to .90)	75 (51 to 90)	75 (64 to 84)	3.00	0.33	0.50
	98	Teacher	>59	.82 (.70 to .94)	79 (54 to 93)	77 (66 to 86)	3.46	0.27	0.56
SDQ*	103	Child	>11	.73 (.63 to .84)	68 (43 to 86)	75 (64 to 84)	2.74	0.42	0.43
	104	Parent	>14	.78 (.67 to .89)	55 (36 to 80)	87 (77 to 93)	4.20	0.52	0.42
	99	Teacher	>7	.80 (.70 to .94)	84 (60 to 96)	71 (64 to 84)	2.93	0.22	0.56
PedsQL†	103	Child	<65	.85 (.77 to .93)	84 (60 to 96)	79 (68 to 86)	3.93	0.20	0.63
	103	Parent	<51	.82 (.72 to .92)	65 (41 to 84)	87 (77 to 93)	4.90	0.40	0.52

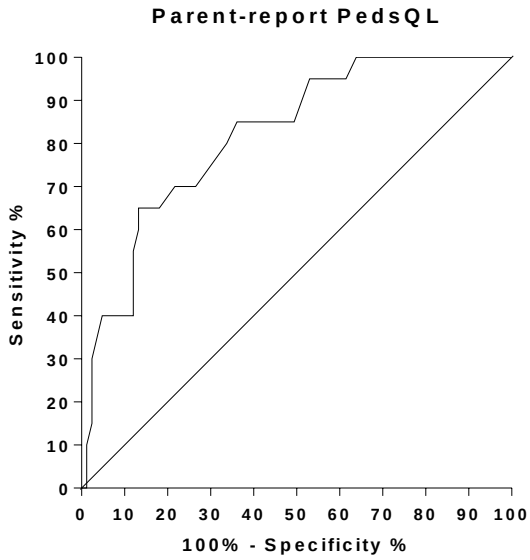
BRIEF, Behavior Rating Inventory of Executive Functioning;[34] SDQ, Strengths and Difficulties Questionnaire;[35] PedsQL, Pediatric Quality of Life Inventory;[36] AUC, area under the curve; Sens, sensitivity; Spec, specificity; LR+, likelihood ratio for a positive test; LR-, likelihood ratio for a negative test; J, Youden Index. All AUCs were significant at $p<001$.

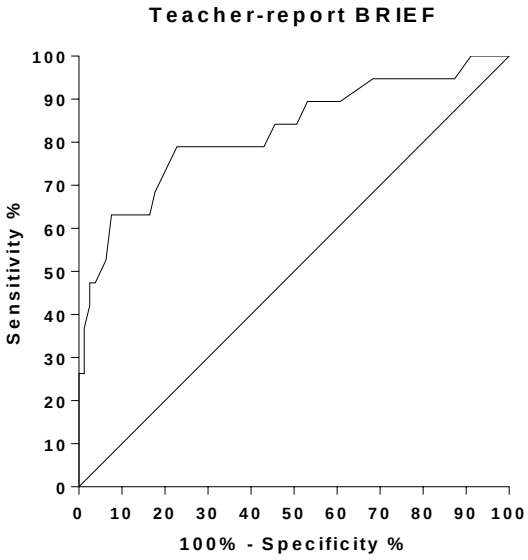
*: higher scores indicate increased dysfunction

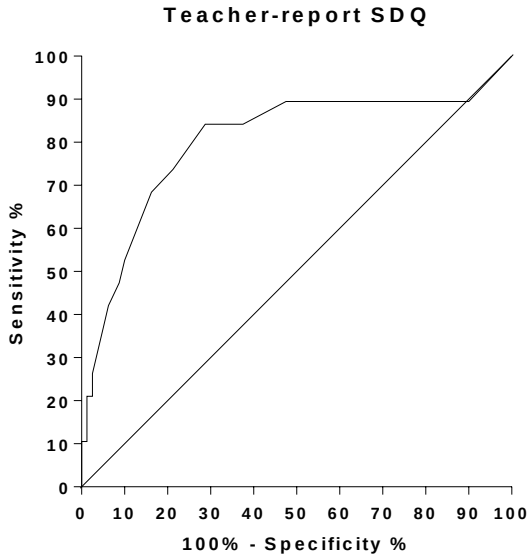
†: higher scores indicate better quality of life

Figure


Child-report PedsQL
Sensitivity %
100% - Specificity %
0
10
20
30
40
50
60
70
80
90
100


Parent-report PedsQL
Sensitivity %
100% - Specificity %
0
10
20
30
40
50
60
70
80
90
100


Teacher-report BRIEF
Sensitivity %
100% - Specificity %
0
10
20
30
40
50
60
70
80
90
100


Teacher-report SDQ
Sensitivity %
100% - Specificity %
0
10
20
30
40
50
60
70
80
90
100

Appendix Table 1. Sensitivity of selected screens for detection of 20 cases of full scale IQ score <80 from a population of 8-14 year old children with and without preceding cerebellar tumors.

		Screening questionnaires			
Patient ID		**Teacher BRIEF cut-off score >59**	**Teacher SDQ cut-off score >7**	**Parent PedsQL cut-off score <51**	**Child PedsQL cut-off score <65**
Medulloblastoma	**105**	+	+	-	missing
	107	+	+	+	+
	109	+	+	+	+
	113	+	+	+	+
	115	+	+	+	+
	118	+	+	-	+
	120	+	+	+	+
	126	+	+	-	-
	127	+	+	+	+
	130	+	+	+	+
	131	-	+	-	-
	136	+	+	+	+
	138	-	-	-	-
	Total +ve	11	12	8	9
Astrocytoma	**203**	+	+	+	+
	212	-	-	+	+
	229	-	-	+	+
	233	missing	missing	+	+
	232	+	+	+	+
	235	+	+	-	+
	Total +ve	3	3	5	6
Non-tumor	**307**	+	+	-	+
	Total +ve	1	1	0	1
Grand Total +ve		16	16	13	16

BRIEF, Behavior Rating Inventory of Executive Functioning;[34] SDQ, Strengths and Difficulties Questionnaire;[35] PedsQL, Pediatric Quality of Life Inventory;[36] FSIQ, full scale IQ; SD, standard deviation; +, screen positive; -, screen negative; +ve, positive