



Computerized assessment of neuropsychological functioning in pediatric brain tumor patients

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Received: 8 December 2024 / Accepted: 16 January 2025

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Abstract

Purpose Advances in multidisciplinary treatment of childhood brain tumors have significantly prolonged survival and reduced treatment-related complications. This makes the accessibility of digital neurocognitive assessment an important issue in the post-pandemic era.

Methods Twenty pediatric brain tumor patients were recruited between August 2023 and August 2024, and a total of eight standardized Cambridge Neuropsychological Test Automated Battery (CANTAB) tests targeting executive function, memory, and attention were applied on a digital system. Subjects with test data exceeding the 5th and 95th percentile ranges were defined as outlier in this context. Three domains (DMS, PAL, SWM) of the normative data for adult patients provided by CANTAB test were used for comparison. Mann-Whitney U test was used to compare differences in treatment modalities and age groups.

Results Four patients (4/20, 20%) exhibited impairments across four to six cognitive domains, with more than 14 sub-items falling outside the 5th and 95th percentiles. Another 7 patients (7/20, 35%) had impairments confined to a single domain, even though 4 out of 7 (57%) had a total IQ above 100. The subtle neurocognitive impairment of different domains can be effectively identified by automatic digital threshold analysis and reasonably associated with clinical characteristics. The normative data provided by the CANTAB battery for adult populations further enhances the accuracy of detecting neuro-functional impairments.

Conclusion The CANTAB test was shown to be an evaluable and user-friendly neurocognitive assessment tool for post-treatment follow-up in pediatric patients with brain tumors.

Keywords Cambridge Neuropsychological Test Automated Battery (CANTAB) · Neuropsychological assessment · Pediatric brain tumor · Neurocognitive dysfunction · Executive function test

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Introduction

Pediatric patients with brain tumors (BTs) are at high risk for neurocognitive impairment, either due to the tumor itself or because of treatments such as surgical intervention, chemotherapy or radiotherapy [1–3]. Several studies have shown harmful effects of radiation therapy on neurocognitive function, particularly in younger patients [3–8]. Some studies indicated that certain patients experience neurological dysfunction prior to treatment, which may be related to the tumor's location [3, 9, 10]. These patients also often exhibit varying degrees of emotional and behavioral problems, leading to poor social adaptation and academic performance, which continue to profoundly affect their lives after treatment [9, 11]. Another study found that neurocognitive function declined significantly five years after radiotherapy, with factors such as younger age at diagnosis and treatment, tumor location in a susceptible brain area, and an intensive treatment process contributing to worse performance [3].

There have been various advances in the treatment of childhood brain tumors in recent years, aimed at extending patient survival rates and reducing treatment side effects [3, 6]. Numerous studies have focused on assessing neurocognitive function, with the goal of evaluating patients' long-term neurological prognosis and improving their quality of life [1, 2, 4–8, 11–25]. In recent decades, online assessment systems have been developed [6, 26]. During the COVID-19 outbreak, the demand for online assessments grew rapidly. This approach offers many benefits, particularly in areas with a shortage of professionals, as well as for patients who may find it inconvenient to travel to and from the hospital.

The Cambridge Neuropsychological Test Automated Battery (CANTAB) is a computerized neuropsychological assessment battery developed in the 1980s by Professors Trevor Robbins and Barbara Sahakian at the University of Cambridge, inspired by their research on neuropsychological deficits in neurological and psychiatric conditions. CANTAB is a highly credible cognitive assessment tool, offering advantages such as sensitivity to subtle changes [27], reduced biases, and efficiency in administration compared to traditional paper-and-pencil tests [28]. It is especially valuable for clinical and research settings requiring precision and scalability. CANTAB offers a range of tasks designed to evaluate patients' executive functions, memory, and attention—areas that are of significant concern for families regarding cognitive function prognosis.

In recent years, several studies have utilized the CANTAB battery to assess pediatric brain tumor patients for monitoring cognitive function in children and evaluating the effectiveness of rehabilitation programs aimed at enhancing cognitive abilities [29–31]. One study uses 5 CANTAB subtests, including Motor Screening (MOT), Pattern

Recognition Memory (PRM), Spatial Span (SSP), Stocking of Cambridge (SOC), Spatial Working Memory (SWM), and Rapid Visual Information Processing (RVP) to evaluate cognitive function of patients who had survived posterior fossa tumors. The study found that the CANTAB tests were sensitive to the effects of rehabilitation training, particularly in areas of working memory and processing speed. For example, the RVP test, which measures speed of processing, showed significant improvement after training [29].

The other study utilized 5 CANTAB subtests including Rapid Visual Information Processing (RVP) and Match to Sample Visual Search for attention (MTS), Simple Reaction Time (SRT) and Choice Reaction Time (CRT) for processing speed, and Delayed Matching to Sample (DMS) for short-term memory. The key finding was that group exercise training significantly decreased reaction time (RT), while there was no significant change in accuracy. This reduction in RT was associated with increased white matter fractional anisotropy (FA) and hippocampal volume, and these effects were observed with carryover after training ended. Notably, the group training setting showed more cognitive benefits than combined group/home-based training. These results suggest that CANTAB is a valuable tool for monitoring cognitive function and evaluating the effectiveness of cognitive rehabilitation in this population [31].

In order to evaluate the accessibility of digital CANTAB neurocognitive testing in pediatric brain tumor patients at MacKay Children's Hospital, we administered a total of eight tests focusing on executive function, memory, and attention during the follow-up post-treatment periods. In addition, we collected comprehensive clinical information from the patients and conducted analyses of the test outcomes. The primary objective of this study is to verify the applicability of CANTAB for evaluating the neurocognitive functions of pediatric brain tumor patients and to identify potential neurocognitive dysfunction in this population receiving various treatment modalities.

Materials and methods

After being approved by the Institutional Review Board (IRB No.22MMHIS431e), the study enrolled 20 stable cases of children with brain tumors after treatment between August 2023 and August 2024. This assessment was performed in an independent outpatient setting. Each assessment lasted about one and a half hours. The participating children were accompanied by a well-trained assistant and reminded verbally when they needed help. The Computerized Cambridge Neuropsychological Test Automated Battery (CANTAB) cognitive assessment is a digital system and comprises a total of eight standardized tests targeting executive function,

memory, and attention. The testing system was purchased and available for limited patient licensing, which included 8 specific assessments of delayed matching to sample (DMS), paired associates learning (PAL), pattern recognition memory (PRM), and verbal recognition memory (VRM) for the memory domain; multi-tasking test (MTT), spatial working memory (SWM), and stop signal task (SST) for executive function; and rapid visual information processing (RVP) to evaluate attention. A detailed description of the CANTAB subtest results is provided in Supplementary Table 1. The diagram in Fig. 1 includes images of three CANTAB subtests, highlighting key components of the assessment process. The clinical neurological symptoms and signs, detailed demographics data and available intelligence test results were subsequently analyzed.

When the participating children completed the CANTAB subtests on an iPad, following auditory instructions provided by the system, the assistant accompanied them to ensure the smooth administration of the tests. The CANTAB system automatically generated the test results.

Statistical analysis

The demographic data of all patients were presented as descriptive statistics, which including age, sex, type and location of tumors, and treatment modalities such as hydrocephalus management, chemotherapy, radiotherapy, and surgical intervention for tissue confirmation. Seventeen patients had available IQ test values which were recorded. For each subset of data of CANTAB test results, we calculated the median, 25th and 75th percentiles, as well as the 5th and 95th percentiles as a reference benchmark. Subjects with test data exceeding the 5th and 95th percentile ranges were defined as outliers in this context. The units mentioned in the text are as follows: milliseconds (ms) for response latency, percentage (%) for accuracy or error rates, and number for counts of correct responses or errors. Given the non-homogeneous distribution of the data, to compare two groups such as those with or without surgical biopsy, with

or without chemotherapy, with or without radiotherapy, age ≥ 18 years or < 18 years, age ≥ 16 years or < 16 years, and with or without surgery due to hydrocephalus based on CANTAB results, we employed the Mann-Whitney U test for comparison. All the analyses were conducted using SPSS Statistics for Windows, version 26.0.

Results

Clinical characteristics

The basic patient profile is presented in supplementary Table 2. The cohort consisted of 16 males and 4 females, with a median age of 13.5 years (range 6 to 20) at the time of diagnosis and a median age of 16 years (range 10 to 22) for the first assessment. The median interval between diagnosis and the first evaluation was 2 years (range 1 to 7), indicating that 65% of patients underwent first testing in less than 2 years after diagnosis. Tumor types included 10 patients with germ cell tumors, 4 with craniopharyngiomas, 2 with gangliogliomas, and 4 with other high-grade (grade 3 and grade 4) brain tumors. Tumors were primarily located in the suprasellar region, pineal area, diencephalon, and mid-brain. Notably, 7 out of 20 patients (35%) required surgical intervention due to hydrocephalus, and 14 patients out of 20 patients (70%) underwent surgery for tissue confirmation.

Regarding treatment, 14 patients (14/20, 70%) received chemotherapy, and 16 patients (16/20, 80%) underwent radiotherapy, with details of the radiation field presented in Table 1.

Results of CANTAB test for patients with brain tumor

We summarized several sub-items across each domain, presenting the median and 25th to 75th percentile values in Table 2. To identify patients with prominent neurocognitive impairments, we also included the 5th and 95th

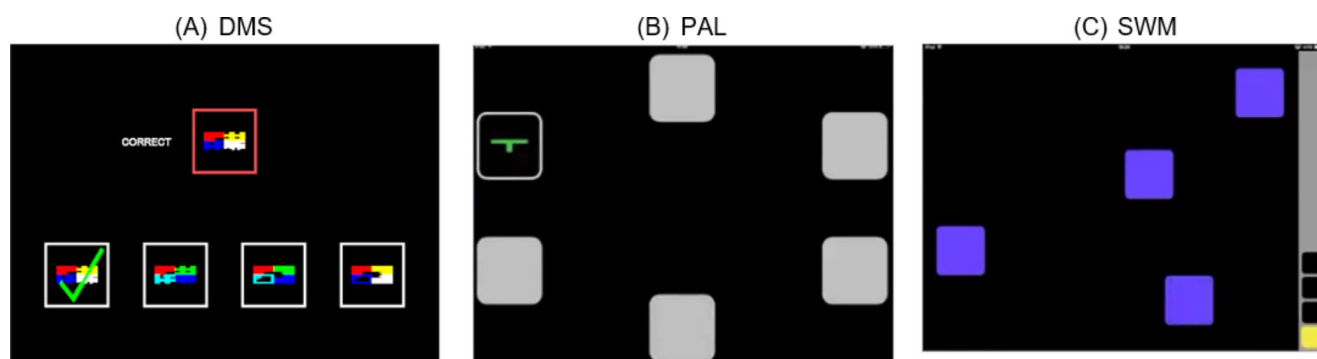


Fig. 1 Photographs of 3 CANTAB subtests. (A) the DMS task, (B) the PAL task, and (C) the SWM task, respectively. DMS: Delayed Matching to Sample; PAL: Paired Associates Learning; SWM: spatial working memory; Adapted with permission from Cambridge Cognition

Table 1 Demographic data of the enrolled 20 subjects

Age at diagnosis, median, range (years)	13.5 [6–20]
Age at first evaluation, median, range	16 [10–22]
Interval between diagnosis and first evaluation, median, range	2 [1–7]
sex, male to female	16 to 4
Type of tumor (N, %)	
Germ cell tumor	10 (50.0%)
Craniopharyngioma	4 (20.0%)
Ganglioglioma	2 (10.0%)
High grade tumor, grade 3 and 4	4 (20.0%)
Tumor location (N, %)	
Suprasellar	9 (25.0%)
Pineal region	7 (19.4%)
Diencephalon	7 (19.4%)
Brainstem	6 (16.7%)
White matter	3 (8.3%)
Cerebellum	2 (5.6%)
Basal ganglia	1 (2.8%)
Cortex	1(2.8%)
Treatment (N,%)	
Hydrocephalus with shunting	7 (35.0%)
Surgery	14 (70.0%)
Chemotherapy	14 (70.0%)
Radiotherapy	16 (80.0%)
Radiation fields (N, %)	
Primary	5 (25.0%)
WVI+primary site	4 (20.0%)
WVI	3 (15.0%)
CSI+primary site	2 (10.0%)
WBI+primary site	2 (10.0%)
No radiotherapy	4 (20.0%)
Radiation dose, mean, range (Gy)	30.6 ± [23–66]

Abbreviation: CSI: craniospinal irradiation; WBI: whole brain irradiation; WVI: whole ventricle irradiation

percentile values, highlighting sub-items that fell outside these thresholds.

Our primary goal was to demonstrate that the test effectively reveals neurocognitive vulnerabilities in patients and aligns with clinical symptoms. Four patients exhibited impairments across four to six cognitive domains, with more than 14 sub-items falling outside the 5th and 95th percentiles, as detailed in Table 3, with further descriptions provided in the following sections.

Among the remaining 16 patients, seven had impairments confined to a single domain, which included:

- Four patients with deficits in executive function (MTT, SST, SWM),
- Two patients with deficits in visual memory and attention (DMS),
- One patient with deficits in verbal memory (VRM).

Of these seven patients, four (57%) had a total IQs above 100 (ranging from 102 to 107), demonstrating the test's sensitivity in detecting subtle but clinically significant neurocognitive vulnerabilities, even in patients with higher baseline cognitive abilities. A detailed description of the CANTAB subtest results for these patients is provided in Supplementary Table 3.

Summary of clinical characteristics and CANTAB data in significantly impaired patients

Case 1: patient number 5

This 20-year-old male was diagnosed with a germinoma located in the suprasellar and pineal regions in January 2023. He underwent six cycles of chemotherapy using the JEB protocol, followed by whole-ventricle radiotherapy (30 Gy) completed in June 2023. His symptoms included blurred vision and dizziness, with diabetes insipidus and panhypopituitarism subsequently identified through thorough evaluation.

Academically, his performance was in the lower-middle range, and his studies were previously interrupted. Cognitive assessment revealed a total IQ of 55, with a working memory score of 65 (PR=1) and a processing speed score of 50 (PR<0.1).

The CANTAB results demonstrated widespread impairments across memory, attention, processing speed, and executive function. The patient exhibited slower and more variable response times, increased error rates, and reduced accuracy across multiple tasks. These findings suggest significant difficulties in efficiently retaining, recalling, and processing information. The observed deficits may be associated with dysfunction in hippocampal regions (memory), attentional control networks, or frontal lobe-mediated executive processes.

Case 2: patient number 7

This 12-year-old boy was diagnosed with a multilobulated craniopharyngioma involving the suprasellar region and septum pellucidum in March 2018. He underwent five surgical interventions and gamma knife radiotherapy. The patient had hypothyroidism, diabetes insipidus, and adrenal insufficiency, all managed with medication. He also presented with left eye blindness and a right-eye visual field defect affecting the lateral 1/4. Additional ocular findings included optic atrophy (OS) and myopia with myopic astigmatism (OU).

Neurocognitive evaluation revealed widespread impairments across memory, attention, and executive functions. Poor performance in the Delayed Matching to Sample

Table 2 Results of CANTAB test for patients with brain tumor

Assessment	Median (P25 – P75)	(P5 – P95)
DMS		
Mean Choices to Correct	1.1 (1.05–1.2)	(1–1.59)
Median Correct Latency	2651 (2000.75–3326.88)	(1251.83–3767.55)
Mean Correct Latency	2875.26 (2329.74–3419.91)	(1546.32–4094.23)
Percent Correct		
(simultaneous presentation and all delays)	90 (80–95)	(60.75–100)
(0 s delay)	100 (80–100)	(61–100)
(4 s delay)	90 (80–100)	(41–100)
(12 s delay)	80 (65–100)	(40–100)
(all delays)	87 (80–98.25)	(54–100)
(simultaneous)	100 (80–100)	(61–100)
Probability of Error Given Correct	0.12 (0.01–0.25)	(0–0.41)
Probability of Error Given Error	0 (0–0.24)	(4 missing data due to no errors)
Total Correct	18 (16–19)	(12.15–20)
MTT		
Reaction latency (mean) for correct trial	582.29 (527.59–638.24)	(401.66–712.19)
Reaction latency (median) for correct trial	521.75 (489.25–596)	(373.48–653.25)
Reaction latency (SD) for correct trial	209.42 (157.23–223.57)	(75.25–343.86)
Mean response latency (direction of arrow)	534.75 (483.98–572.67)	(428.09–692.65)
Mean response latency(direction of stimulus)	612.91 (580.98–698.02)	(452.79–737.08)
Standard deviation of response latency (both rules)	214.58 (163.18–253.86)	(76.33–391.20)
Standard deviation of response latency (incongruent trials)	191.64 (163.74–238)	(70.1–400.18)
Median response latency (side blocks)	404.25 (373.13–452.25)	(339.23–654.95)
Median response latency (side of screen)	466.75 (412.63–523)	(340.5–670.15)
Multitasking block errors	9 (5.25–15.25)	(1.05–21.8)
Multitasking cost (median)	165.75 (101.13–213.75)	(–15.15–298.65)
Side block errors	0 (0–1)	(0–3.9)
Single Task block errors	2 (1.25–3.75)	(0–10.85)
Total correct	146.5 (140.25–154.25)	(132.1–157.95)
PAL		
First Attempt Memory Score	16 (14.25–17)	(7.2–19.9)
Total Attempts	6 (5–7)	(4.05–7.95)
Total Errors (Adjusted)	5.5 (3.25–7.75)	(0.1–43.6)
PRM		
Correct Latency (SD)-delayed choice	574.28 (363.33–998.29)	(211.56–1775.87)
Correct Latency (SD)-immediate choice	432.51 (278.86–1026.2)	(110.16–1939.08)
Mean Correct Latency-delayed choice	1836.96 (1607.8–2223.68)	(1026.45–3389.28)
Mean Correct Latency-immediate choice	1687.69 (1494.75–1965.95)	(1044.73–4417.29)
Median Correct Latency-delayed choice	1716.25 (1529–1996.13)	(968.25–2760.73)
Median Correct Latency-immediate choice	1517.5 (1373.88–1906.75)	(1034.35–4172.95)
Percent Correct Delayed	87.5 (77.08–91.67)	(50.83–100)
Percent Correct Immediate	100 (91.67–100)	(75.42–100)
RVP		
A prime	0.97 (0.97–0.99)	(0.93–0.99)
Response Latency (SD)	103.2 (68.41–141.57)	(41.83–246.54)
Median Response Latency	391.75 (354–439.5)	(273.75–570.05)
Total False Alarms	4.5 (1–7.75)	(0–50.9)
Total Hits	50 (46–53)	(42.05–54)
Total Misses	4 (1–8)	(0–11.95)
SST		
Direction Errors: Go Trials	2.5 (0.25–7.5)	(0–47.6)
Direction Errors: Stop Trials	40 (37.25–44)	(33.05–56.5)
Median RT: Go Following Stop	593.25 (504–649.25)	(580.78–750.23)
Missed Trials	4 (2–7.25)	(0.05–37.55)
Stop Signal Reaction Time	265.25 (249.13–288.4)	(169.81–424.65)

Table 2 (continued)

Assessment	Median (P25 – P75)	(P5 – P95)
SWM		
Between Errors (4,6,8 boxes)	10 (1.25–16.75)	(0–24.8)
Between errors 8 boxes	5.5 (0.25–10)	(0–18.9)
Strategy (6–8 boxes)	8 (7–10)	(3–11.95)
Strategy (6–12 boxes)	15 (11.25–17.75)	(6–22.8)
Total Errors	10 (1.25–16.75)	(0–24.8)
VRM		
Delayed: Correct to Distractors	16.5 (14.25–17)	(10–18)
Delayed: Correct to Stimuli	16 (14.25–17)	(9–17.95)
Delayed: Incorrect to Distractors	1.5 (1–3.75)	(0–8)
Delayed Recognition	31 (28.5–33)	(24.1–34.95)
Free Recall	5 (3–6)	(2–13.7)
Free Recall: Novel Words	0 (0–1)	(0–2.95)
Free Recall: Perseverations	0(0–0)	(0–2.9)
Immediate: Correct to Distractors	17 (14.25–18)	(10.05–18)
Immediate: Correct to Stimuli	15 (14–16)	(12–18)
Immediate: Incorrect to Distractors	1 (0–3.75)	(0–7.95)
Immediate Recognition	32 (29–33)	(24.15–35)

Abbreviation: DMS: Delayed Matching to Sample; MTT: Multitasking Test; PAL: Paired Associates Learning; PRM: Pattern Recognition Memory; RVP: Rapid Visual Information Processing; SST: Stop Signal Task; SWM: Spatial Working Memory; VRM: Verbal Recognition Memory; P25: 25 percentile; P75: 75 percentile; P5: 5 percentile; P95: 95 percentile

(DMS), Paired Associates Learning (PAL), and Rapid Visual Processing (RVP) tests, when compared to other patients, highlighted deficits in cognitive functioning. These impairments included slowed and inconsistent response times, difficulties in retaining and recalling information, increased susceptibility to errors, and impulsive responses. The observed pattern suggested dysfunction in the hippocampal-dependent memory processes, prefrontal cortex-mediated executive functions, and attentional control networks.

The patient's left eye blindness and right-eye visual field defect further compromised visual processing capabilities, potentially exacerbating difficulties in cognitive tasks requiring efficient visual input and integration.

Case 3: patient number 8

This 20-year-old male was diagnosed with a suprasellar germinoma in June 2021. His symptoms included blurred vision, dizziness, headaches, vomiting, tremor, unsteady gait, weight loss, diabetes insipidus, and right oculomotor nerve palsy caused by increased intracranial pressure due to obstructive hydrocephalus. He underwent surgical intervention followed by six cycles of chemotherapy with the JEB protocol, and subsequently, whole-brain radiotherapy to a total dose of 31 Gy. He graduated from vocational high school and is currently employed at a convenience store. His total IQ was assessed at 77.

Neurocognitive evaluation revealed impairments in sustained attention, response inhibition, working memory, and episodic memory. The patient exhibited increased variability

in response latencies, heightened susceptibility to interference, and poor performance on tasks assessing memory and multitasking abilities. These findings highlight difficulties in cognitive flexibility, inhibitory control, and memory consolidation, suggesting dysfunction in frontal and hippocampal regions critical for these processes.

Case 4: patient number 17

This 14-year-old girl was diagnosed with a germinoma in February 2020, involving the basal ganglia, corona radiata, corpus callosum, septum pellucidum, bilateral frontal horn ventricular walls, internal capsule, hypothalamus, optic chiasm, and upper infundibular stalk. She had long-term symptoms, including growth retardation, diabetes insipidus, declining academic performance, and impulsive behavior with hyperactivity. Her recent symptoms prior to diagnosis included blurred vision, dizziness, headaches, and vomiting.

The patient underwent six cycles of chemotherapy with the JEB protocol, followed by whole-brain proton radiotherapy to a total dose of 54 Gy. She has panhypopituitarism and ADHD, both requiring medical management. She received traditional neuropsychological assessment which revealed notable deficits in multitasking, disinhibited behavior, and impairments in both visual and verbal memory, particularly in immediate recall and recognition tasks.

CANTAB testing indicated significant impairments across multiple cognitive domains, including processing speed, attention, response inhibition, working memory, and episodic memory. The results showed increased response

Table 3 Patients with CANTAB results outside the 5th or 95th percentile

Patient number	CANTAB results falling outside 5 percentile or 95 percentile (ms)	CANTAB evaluation conclusion	Clinical description
5	<p>DMS: Correct Latency Standard Deviation (SD) (simultaneous and all delays): 2245.0333 Correct Latency(SD) (simultaneous): 3819.5266 Median Correct Latency (4 s delay):5954 Mean Correct Latency (4 s delay):5654.3333 Mean Correct Latency (simultaneous): 4787 PAL: Total Errors: 17 Total Errors 8 Patterns: 17 PRM: Correct Latency (SD)-delayed forced-choice: 1787.99 Correct Latency (SD)-immediate forced-choice: 1947.83 Mean Correct Latency-delayed forced-choice: 3418.92 Mean Correct Latency-immediate forced-choice: 4467.55 Median Correct Latency-delayed forced-choice: 2786.5 Median Correct Latency-immediate forced-choice: 4238 RVP: Median Response Latency: 561.5 Probability of False Alarm: 0.0946 Total False Alarms: 51</p>	Visual memory impairment, attention deficit	Intellectual disability (total IQ=55, working memory 65 (PR1), processing speed 50(PR<0.1))
7	<p>DMS: Mean Choices to Correct: 1.6 Percent Correct (simultaneous presentation and all delays): 60 Percent Correct (12 s delay): 40 Percent Correct (4 s delay): 40 Percent Correct (all delays): 53 Probability of Error Given Correct: 0.4167 Total Correct (simultaneous presentation and all delays): 12 Total Correct (12 s delay): 2 Total Correct (4 s delay): 2 Total Correct (all delays): 8 Total Errors (simultaneous and all delays): 8 Total Errors (all delays): 7 Error (simultaneous and all delays, incorrect colour): 5 Error (all delays, incorrect colour): 5 Error (simultaneous and all delays, distractor): 2 Error (all delays, distractor): 2 MTT: Side block errors: 4 PAL: First Attempt Memory Score: 7 Number of Patterns Reached: 6 Total Attempts 2 Patterns: 2 Total Attempts 6 Patterns: 4 Total Errors: 17 Total Errors 2 Patterns: 1 Total Errors 6 Patterns: 16 Total Errors (Adjusted): 45 Total Errors 2 Shapes (Adjusted): 1 Total Errors 6 Shapes (Adjusted): 16 Total Errors 8 Shapes (Adjusted): 28 RVP: Response Latency (SD): 250.0886 Probability of False Alarm: 0.0909 Total False Alarms: 49</p>	Visual memory impairment, attention deficit	optic atrophy, left eye near blindness, right 1/4 visual field defect

Table 3 (continued)

Patient number	CANTAB results falling outside 5 percentile or 95 percentile (ms)	CANTAB evaluation conclusion	Clinical description
8	DMS: Probability of Error Given Error: 0.5 MTT: Congruent errors: 6 Incongruency cost (mean): 124.29 Standard deviation (SD) of the response latency to the stimulus: 334.31 SD of the response latency (both rules): 391.97 SD of the response latency (incongruent trials): 403.77 SD of the response latency (all corrects): 344.98 SST: Mean Failed Stop RT Increases: 0 SWM: Between errors 4 boxes: 3 Total errors 4 boxes: 3 VRM Delayed: Correct to Distractors: 10 Delayed: Incorrect to Distractors: 8 Delayed Recognition: 24 Free Recall: Perseverations: 3	Executive function impairment (Prominent), Memory function impairment (verbal more prominent), attention deficit	Boarderline cognitive delay (total IQ: 77, language comprehension: 70, working memory: 75)
17	MTT: SD of the response latency (congruent): 338.2 Mean response latency to the direction of the arrow: 694.35 Median response latency to the direction of the arrow: 670.5 SD of the response latency to the direction of the arrow: 211.74 SD of the response latency to the direction of the stimulus: 325.96 Mean response latency to the side of the screen: 690.03 Median response latency (side blocks): 654 SD of the response latency to the side of the screen: 301.54 Median response latency (side of screen): 654 Mean response latency (single task blocks): 692.22 Median response latency (single task blocks): 670 SD of the response latency (single task blocks): 258.3 MTT Multitasking cost (median): -16 Commission errors: 1 PRM: Percent Correct Immediate: 75 RVP: Median Response Latency: 570.5 SST: Mean Failed Stop RT Increases: 0 Missed Trials: 39 SWM: Between errors 8 boxes: 19 Total errors 8 boxes: 19 VRM: Delayed: Correct to Stimuli: 9	Executive function impairment (prominent), Memory function impairment (verbal and visual), attention deficit	Prominent verbal and visual memory deficit (<0.1 percentile), hyperactive and inattention, total IQ = 100

variability, slower reaction times, and higher error rates in multitasking and memory tasks. These findings suggested dysfunction in the prefrontal cortex, hippocampus, and associated neural networks. The patient exhibited difficulties in sustaining attention, suppressing impulsive responses, managing working memory, and retrieving information efficiently, consistent with her clinical history and underlying condition.

These case examples highlight the sensitivity of the CANTAB test to specific neurocognitive impairments that align with clinical symptoms. This test's ability to identify

neurocognitive dysfunction, particularly in areas of impulsivity, attention, and memory, makes it a valuable tool for capturing the effects of neurological impairments on cognitive performance.

Comparison of normative dataset and age factors in CANTAB Testing

This test includes normative data for subjects over 18 years across several items in 3 domains (DMS, PAL, SWM) which were listed in Table 4. Comparative values were available

Table 4 The comparison with CANTAB test provides normative data in adult patients

Assessment Case number	DMS					PAL		SWM		
	Percent Correct		(4 s delay)	(all delays)	(simultaneous)	Probability of Error Given Error	First Attempt Memory Score	Total Errors (Adjusted)	Between Errors (4,6,8 boxes)	Strategy (6–8 boxes)
(0 s delay)	(12 s delay)									
3	100 (99th)	100 (99th)	100 (99th)	100 (99th)	100 (99th)	.	16 (77th)	4 (80th)	0 (99th)	4 (80th)
5	80 (30th)	80 (39th)	60 (12th)	73 (17th)	80 (8th)	0.2 (26th)	16 (77th)	17 (48th)	1 (70th)	7 (37th)
8	100 (99th)	80 (39th)	80 (32th)	87 (57th)	100 (99th)	0.5 (5th)	14 (59th)	8 (68th)	25 (1st)	11 (5th)
13	100 (99th)	100 (99th)	100 (99th)	100 (99th)	100 (99th)	.	17 (84th)	4 (80th)	0 (99th)	3 (91th)
15	80 (30th)	60 (15th)	80 (32th)	73 (17th)	80 (8th)	0.25 (23th)	17 (84th)	3 (83th)	0 (99th)	7 (37th)
16	100 (99th)	100 (99th)	100 (99th)	100 (99th)	100 (99th)	.	15 (46th)	6 (50th)	2 (57th)	8 (20th)

Abbreviation: DMS: Delayed Matching to Sample; PAL: Paired Associates Learning; SWM: Spatial Working Memory

for six patients, three of whom (Patient numbers 3,13,16) scored within the normal range. Two patients (Patient numbers 5 and 15) with intellectual disability (total IQ scores of 55 and 63) displayed similar patterns of compromised performance in the DMS domain.

Additionally, patient number 8, with an IQ score of 77, showed a DMS Probability of Given Error of 0.5 (5th percentile), which indicated the patient had a 50% chance that if he made one error, he would make another on a subsequent similar trial, which suggested challenges with learning from mistakes, adapting strategies, or retaining information. The SWM Between Errors (4,6,8 boxes) revealed 25 (1st percentile) which indicated difficulty in recalling previously searched locations, leading to repeated searches of the same box, suggesting impairments in working memory or attention. SWM Strategy (6–8 boxes) revealed 11 (5th percentile) which suggested a more haphazard or random search approach that reflected poor planning, strategy use, or difficulty remembering previously searched locations. According to these findings, the patient had cognitive deficits in working memory, attention, and executive function.

As previous literature shows [32–34], our comparative analysis of the CANTAB test results reflects age-related variations in neurocognitive processing, particularly in areas related to reaction latency and error correction. Compared with other groups for treatment modalities, where the disproportionate case ratios might introduce bias and the analysis results showed no significant differences, the analysis revealed notable differences between these two age groups in specific subtests. This finding further supports the notion that neurocognitive functions mature over time. However, it is not yet possible to determine whether these differences reflect distinct maturation timelines for specific abilities, and further data are likely needed to clarify this. There were significant performance differences between patients over 18 years of age and those younger than 18 listed in Supplementary Tables 4 and summarized significant differences between those aged over 16 years of age and younger than 16 listed in Supplementary Table 5.

Discussion

The CANTAB test has been utilized across various neuropsychological disorders in both adults [35–37] and adolescents [38, 39], with increasing applications in children [32, 33, 38–40], including Attention Deficit Hyperactivity Disorder (ADHD) [41–43] and Autism Spectrum Disorder (ASD), even for pediatric brain tumor patients in recent years [29–31]. While normative values for adults has been established [44], studies addressing normative values for children remain sporadic [32, 34, 38, 39]. This study aims to broaden application of the CANTAB test to assess multiple domains of neurocognitive function—including attention, executive function, and memory—specifically in pediatric brain tumor patients.

We analyzed the raw data from 20 patients and identified notable disparities exceeding age-related expectations. To minimize the risk of over-interpretation, we defined the 5th and 95th percentile ranges and flagged values falling outside this range. Additionally, we recorded the number of cognitive domains in which each patient exhibited significantly abnormal results compared to others. These abnormalities indicated relatively weaker abilities and highlighted functional deficits that warranted attention.

We analyzed the neurocognitive data of patients by comparing groups based on treatment modalities (radiation or chemotherapy), presence of hydrocephalus, surgical intervention, and age at diagnosis. Statistical differences were notably observed only within the age-at-diagnosis comparisons, revealing that late adolescents demonstrated higher accuracy and shorter reaction times compared to younger patients. Conversely, during the Pattern Recognition Memory test, older patients exhibited longer correct latencies. Clinical observation indicated that adults tended to take more time to confirm their recognition of patterns, while responding more quickly on time-sensitive tests such as RVP, SST, and MTT. Notably, 17 out of 20 patients displayed at least one sub-item result that fell outside the 5th or the 95th percentile, with five of those patients having

total IQ scores ranging from 100 to 107, and all sub-item scores above 90. This suggests that the CANTAB test may effectively reveal underlying weaknesses or neurocognitive dysfunction.

Although normative data for children have not yet been fully established, analyzing and comparing neurocognitive function between patients can still provide valuable reference points for clinicians and parents. By comparing age-related differences, clinicians can further clarify the relationship between neurocognitive functions and developmental milestones.

Special attention should be given to younger patients, who require continued education and cognitive training alongside their treatment. This dual approach of therapeutic and educational support can help foster better neurocognitive outcomes, enhancing their potential for learning and adaptation as they grow. Additionally, formal recognition of neurocognitive dysfunction can assist families in accessing governmental education and rehabilitation resources to help children with brain tumors recover [45–47]. We also evaluate improvements in neurocognitive function by tracking and assessing changes following disease treatments and rehabilitation [29–31].

All patients reported positive feedback on the assessment experience, noting that the tablet was user-friendly, instructions were clearly explained, and the testing duration was appropriate for their return visit. For patients experiencing academic difficulties without available evidence on IQ tests, the subclinical neurocognitive dysfunction results indicated by CANTAB can provide valuable information for parents and guidance for teachers to address specific weakness.

Our findings show that patients with multiple domains exhibiting marked weaknesses tend to align more closely with their clinical conditions. This provides a dual benefit: first, it serves as a reference for longitudinal follow-up, offering insights into the potential clinical burden posed by these vulnerabilities. Second, as the patient cohort expands, it allows for further exploration of the relationship between these deficits and other clinical data.

Limitation

Despite the evident utility of the CANTAB assessment for our patient cohort, several limitations warrant consideration. Our sample size was relatively small and exhibited an asymmetric diagnostic distribution, predominantly comprising germ cell tumor patients. Furthermore, longitudinal follow-up provides more substantial evidence of progression of neuropsychological outcomes over time. In addition, the challenge of multiple comparisons in this rare population necessitates careful consideration of numerous clinical variables. This study did not establish sex-specific

inclusion criteria but faithfully recorded the sex of patients who underwent testing during the inclusion period. According to the literature, pediatric brain tumor cases generally show a male predominance, with a ratio of approximately 1.33:1 [48]. Consequently, no specific comparisons based on sex were conducted in this study.

Prospective data collection is currently ongoing, and we anticipate uncovering significant findings regarding post-treatment outcomes beyond our current understanding.

Conclusion

In conclusion, this study represents our experience of utilizing the CANTAB computerized assessments to evaluate attention, memory, and executive functioning in pediatric brain tumor survivors. With high acceptance rates and valid clinical data, the CANTAB test proves to be an evaluable and highly accessible neurocognitive assessment tool for post-treatment follow-up in this population.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11060-025-04945-x>.

Acknowledgements We acknowledge that this research was sponsored by MacKay Memorial Hospital (grant number: MMH-112-103) and performed by the MacKay Pediatric Brain Tumor Team.

Author contributions JY Huang, CS Ho executed study and collected data. TC Yen, HC Liu & JY Hou were in charge of clinical data collection. TY Yen, CC Huang & HC Lao contributed to the management of data analysis. JY Huang, TC Yen, HC Liu & JY Hou, CS Ho & ML Liang wrote the manuscript. CS Ho & ML Liang supervised the project. All authors contributed to the final version of the manuscript.

Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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