

Age, Not Tumor Location, Predicts Early Neurocognitive Impairment After Pediatric CNS Tumor Surgery: A Cross-Sectional Study at a Mexican Tertiary Center

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Case Report

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Abstract

Purpose.

Pediatric CNS tumors are the leading cause of cancer-related mortality in children under 15. Surgery reduces tumor burden but delivers a second neurological insult to a brain already compromised by the lesion. We aimed to characterize early post-surgical neurocognitive profiles and determine whether tumor location or age at surgery predicts deficit severity at one month in a Latin American pediatric cohort.

Methods.

Cross-sectional retrospective study at CMN "20 de Noviembre" (ISSSTE), Mexico City (August 2021 – August 2023). Sixty children aged 6–17 years who underwent CNS tumor resection completed the NEUROPSI brief battery one month post-surgery. Logistic regression models for orientation, selective attention, and working memory were adjusted for age and tumor location (supratentorial vs. infratentorial).

Results.

Mean age was 11.2 years (SD 3.7); 65% were male. One month after surgery, 36.7% scored below normal in orientation, 41.7% in selective attention, and 43.3% in working memory. Tumor location did not predict deficit severity in any domain (all 95% CI crossed null). Each additional year of age independently reduced orientation-deficit odds by 21% (OR 0.79, 95% CI 0.68–0.94, $p = 0.007$); age did not predict selective attention or working memory deficits.

Conclusion.

Tumor location did not predict neurocognitive deficit severity at one month. Younger age was the sole independent predictor of orientation impairment. With deficits exceeding 40% across all domains, these findings support universal early neuropsychological screening regardless of lesion site. Prospective studies with pre-surgical baselines, comprehensive batteries, and longitudinal follow-up are needed.

INTRODUCTION

Pediatric CNS tumors are the most common solid malignancies in children under 15 and the leading cause of cancer deaths in this age group [1, 2]. Surgical resection remains the cornerstone of management—it establishes tissue diagnosis, relieves mass effect, and debulks tumor—but it delivers a second neurological insult to a brain already damaged by the lesion. The cognitive picture at one month post-operatively reflects this dual injury, and its consequences extend well beyond the acute ward:

attention failure, disorientation, and working memory impairment disrupt school reintegration and family functioning before adjuvant treatment begins.

Prospective longitudinal studies in high-income settings have characterized long-term cognitive trajectories across multiple domains and years of follow-up [3, 4]. What those studies cannot establish is whether early deficits—present before radiotherapy or chemotherapy—differ by lesion location in a way that should change post-operative triage. Operationally, the question is not trivial: a location-dependent risk model would justify targeted neuropsychological referral, whereas a location-independent one demands screening for every patient. In Mexican public hospitals, where neuropsychological resources are finite, the distinction carries direct resource-allocation consequences. No study has addressed this question in a Mexican pediatric population.

We enrolled 60 children at CMN "20 de Noviembre" (ISSSTE), Mexico City, and administered the NEUROPSI brief battery—the instrument most widely validated in Mexican pediatric samples—one month after CNS tumor surgery. Our objective was to determine whether supratentorial versus infratentorial tumor location predicted deficit severity in orientation, selective attention, and working memory, and to assess whether age modified that risk.

METHODS

Study Design and Setting

We conducted a cross-sectional retrospective study at CMN "20 de Noviembre" (ISSSTE), a tertiary neurosurgical referral center in Mexico City, covering surgeries performed between August 2021 and August 2023. Data collection began in January 2024, after protocol approval on December 26, 2023 (registry RPI: 746.2023).

Participants

We enrolled children aged 6 years to 17 years 11 months with any CNS tumor who underwent neurosurgical intervention at our center. Exclusion criteria were: unstable systemic comorbidity, severe traumatic brain injury, pre-existing documented neurocognitive impairment, history of psychotropic drug dependence, and incomplete clinical records. Of 78 patients initially identified, 18 were excluded, leaving 60 for analysis (Fig. 1).

Neurocognitive Assessment

A certified neuropsychologist administered the NEUROPSI brief battery (Ostrosky et al., 3rd ed., El Manual Moderno, 2019) one month after surgery [5]. We analyzed three domains: orientation (maximum score 7), selective attention (maximum score 9), and working memory (maximum score 8). Scores were classified as normal, mild-to-moderate deficit, or severe deficit using the instrument's age-stratified

Mexican normative tables. Pre-surgical cognitive status was documented by the neurosurgery team through structured clinical examination immediately before the procedure; the absence of a standardized pre-operative NEUROPSI precludes true change-score analysis—a limitation addressed below.

Tumor Location Classification

We classified tumors as supratentorial (frontal, temporal, parietal, and occipital lesions; $n = 21$) or infratentorial (posterior fossa lesions; $n = 39$). Five patients with isolated temporal lesions were classified as supratentorial based on anatomic location above the tentorium cerebelli. This binary classification is the standard neuroanatomic distinction used in pediatric neuro-oncology outcome studies.

Statistical Analysis

The data was entered into a structured Excel database and analyzed with STATA 16. Continuous variables are reported as mean (SD) or median (IQR) based on normality testing; categorical variables as frequency and percentage. We used one-way ANOVA and chi-square tests (Fisher exact correction for cells with expected count below 5) for between-group comparisons. We fitted logistic regression models for each cognitive domain, first bivariate (location only) then multivariate adjusting for location and age—selected a priori based on prior literature [3, 9]. Additional covariates (sex, tumor volume, educational level, histology) were not included in primary models given event-per-variable ratios below 10 for most domain outcomes [16]; bivariate analyses appear in Supplementary Table S1. We report odds ratios (ORs) with 95% confidence intervals and exact two-tailed p-values ($\alpha = 0.05$). No correction for multiple comparisons was applied; all analyses are hypothesis-generating.

Ethics

The study conformed to the Declaration of Helsinki and NOM-012-SSA3-2012. The Institutional Ethics Committee of CMN "20 de Noviembre" approved the protocol (RPI: 746.2023). Each patient received a unique de-identified code.

Use of Artificial Intelligence Tools During the preparation of this work, the authors used Claude Sonnet 4.6 (Anthropic LLM) solely for the purpose of improving the clarity and fluency of the writing, optimizing the structural organization of the text, and facilitating the organization of bibliographic information. The tool was not used at any stage for idea generation, argument formulation, development of the theoretical framework, selection or interpretation of references, preparation of conclusions, or any other substantive intellectual contribution to the manuscript. All concepts, hypotheses, reasoning, and original content are the sole responsibility of the authors. The authors reviewed, edited, and validated the entirety of the resulting content and assume full responsibility for the integrity and accuracy of the published article. No artificial intelligence tool is listed, nor may be listed, as an author of this work.

RESULTS

Sample Characteristics

Of 78 patients reviewed, 60 met inclusion criteria. Mean age was 11.2 years (SD 3.7); 65% were male. Thirty-four patients (56.7%) attended primary school. Astrocytoma was the most common histological type (25.0%), followed by glioblastoma multiforme (15.0%), medulloblastoma (13.3%), craniopharyngioma (10.0%), ganglioglioma or DNET (10.0%), ependymoma and meningioma (6.7% each), and other or unclassified types (13.3%). Tumor volume had a median of 47,318 mm³ (IQR 2,908–62,510). No pre-surgical neurocognitive deficit was documented in any patient (Table 1).

Table 1
Sample characteristics by tumor location.

Characteristic	Supratentorial (n = 21)	Infratentorial (n = 39)
Age, years – mean (SD)	12.1 (3.9)	10.7 (3.5)
Male sex – n (%)	14 (66.7)	25 (64.1)
Educational level – n (%)		
Primary school	11 (52.4)	23 (59.0)
Secondary school	7 (33.3)	12 (30.8)
High school or above	3 (14.3)	4 (10.3)
Histological type – n (%)		
Astrocytoma	9 (42.9)	6 (15.4)
Glioblastoma multiforme	4 (19.0)	5 (12.8)
Medulloblastoma	0 (0)	8 (20.5)
Ependymoma	2 (9.5)	2 (5.1)
Meningioma	2 (9.5)	2 (5.1)
Craniopharyngioma	1 (4.8)	5 (12.8)
Ganglioglioma / DNET	2 (9.5)	4 (10.3)
Other / unclassified	1 (4.8)	7 (17.9)
Tumor volume, mm ³ – median (IQR)	51,240 (3,800–65,100)	44,890 (2,300–60,420)
Pre-surgical neurological deficit – n (%)	0 (0)	0 (0)

Neurocognitive Outcomes

One month after surgery, 22 patients (36.7%) scored below normal in orientation, 25 (41.7%) in selective attention, and 26 (43.3%) in working memory. Deficit rates did not differ by location group in any domain (all $p > 0.50$; Table 2, Fig. 3). The global NEUROPSI median score was 17 (IQR 11–22) in both groups.

Table 2
Neurocognitive outcomes by tumor location at one month post-surgery.

Cognitive Domain	Supratentorial n = 21	Infratentorial n = 39	Total N = 60	p value
Orientation — below normal, n (%)			22 (36.7)	0.51
Mild-to-moderate deficit	6 (28.6)	11 (28.2)	17 (28.3)	—
Severe deficit	2 (9.5)	3 (7.7)	5 (8.3)	—
Selective attention — below normal, n (%)			25 (41.7)	0.73
Mild-to-moderate deficit	9 (42.9)	13 (33.3)	22 (36.7)	—
Severe deficit	1 (4.8)	2 (5.1)	3 (5.0)	—
Working memory — below normal, n (%)			26 (43.3)	0.84
Mild-to-moderate deficit	10 (47.6)	15 (38.5)	25 (41.7)	—
Severe deficit	0 (0)	1 (2.6)	1 (1.7)	—
NEUROPSI global score — median (IQR)	17 (12–22)	17 (11–22)	17 (11–22)	0.91

Effect of Tumor Location and Age

Tumor location did not predict deficit severity in any cognitive domain in bivariate or multivariate models (Table 3, Fig. 2). Infratentorial tumors carried nominally higher odds for orientation deficit, but confidence intervals were wide and crossed null in all models (bivariate OR 1.80, 95% CI 0.54–6.05; multivariate OR 2.01, 95% CI 0.56–7.23). In the multivariate orientation model—the only globally significant model ($p = 0.014$)—each additional year of age reduced orientation-deficit odds by 21% (OR 0.79, 95% CI 0.68–0.94, $p = 0.007$; Fig. 4). Age did not independently predict selective attention or working memory impairment. The Nagelkerke pseudo- R^2 was 0.12 for the orientation model and 0.01 for both others.

Table 3
Logistic regression models for neurocognitive deficit severity by domain.

Bivariate model	Orientation OR (95% CI)	Selective Attention OR (95% CI)	Working Memory OR (95% CI)	p (orientation)
Infratentorial (vs. supratentorial)	1.80 (0.54– 6.05)	0.64 (0.21–1.96)	0.57 (0.18– 1.80)	0.34
Multivariate model (adjusted for age)				
Infratentorial (vs. supratentorial)	2.01 (0.56– 7.23)	0.61 (0.19–1.96)	0.55 (0.17– 1.82)	0.29
Age, per year increase	0.79 (0.68– 0.94)	0.95 (0.83–1.08)	0.97 (0.85– 1.10)	0.007
Pseudo-R² (Nagelkerke)	0.12	0.01	0.01	—

OR = odds ratio; CI = confidence interval. Reference category: supratentorial. All models adjusted for age and tumor location. Supplementary Table S1 presents bivariate analyses for sex, histological grade, tumor volume, and educational level.

DISCUSSION

Tumor location—supratentorial or infratentorial—did not predict deficit severity in orientation, selective attention, or working memory at one month after CNS tumor surgery. Younger age was the sole independent predictor, and only for orientation: each additional year of age was associated with a 21% reduction in deficit odds (OR 0.79, 95% CI 0.68–0.94, $p = 0.007$). Over 40% of patients showed impaired selective attention or working memory, and those proportions were nearly identical across both location groups.

The null result for location converges with Shortman et al. [7], who found no location effect on neurocognitive outcomes during the first year after diagnosis in 71 children. It diverges from Chieffo et al. [8], who found worse naming and praxis with frontal and thalamic lesions on pre-operative assessment of pediatric supratentorial tumors. The discrepancy is likely explained by the measurement window: pre-operative deficits map onto lesion anatomy because the tumor directly disrupts local circuitry; post-surgical deficits at one month are driven by edema, surgical trauma, anesthetic exposure, and raised intracranial pressure—insults that do not respect anatomic boundaries in the same way.

The protective effect of older age on orientation replicates the direction reported in prospective cohorts. Tonning Olsson et al. [6], followed 69 pediatric brain tumor survivors longitudinally and found that younger age at diagnosis predicted larger reductions in IQ and greater deficits in executive function,

memory, and attention. Mynarek et al., in the HIT 2000 trial of 279 patients, identified age below 4 years as the strongest individual risk factor for domain-specific neurocognitive impairment after posterior fossa tumors [9]. The biological rationale is clear: younger children have less myelinated, more diffusely organized neural networks, so injury during critical windows of synaptic pruning and myelination carries disproportionate risk.

The null result for location should not be read as evidence that location does not matter. This study was designed as an exploratory inquiry. With 60 patients and 22–26 events per domain, we had adequate power only to detect large effects ($OR \geq 3.0$ at 80% power). The wide confidence intervals around location ORs—ranging from 0.35 to 7.23—are fully consistent with true moderate effects that our sample could not exclude. Prospective studies enrolling 150–200 patients with pre-operative baselines would be required to estimate location effects of clinically meaningful magnitude.

Educational level showed a protective association with orientation and working memory in supplementary bivariate analyses—consistent with the literature linking socioeconomic disadvantage and interrupted schooling to worse neurocognitive outcomes in pediatric CNS tumor survivors [14, 15]. This association warrants formal testing in larger samples given its direct implications for rehabilitation planning in Mexican public hospitals.

Tumor histology was not a primary predictor here. Klein [10] reported higher cognitive impairment prevalence in high-grade tumors independent of location. In our sample, 28.3% had high-grade histology, but subgroup analysis was precluded by sample size. The bivariate analyses in Supplementary Table S1 showed a non-significant trend toward higher deficit odds with high-grade histology ($OR\ 1.43\text{--}1.61$ across domains), consistent with this literature but underpowered to confirm.

LIMITATIONS

Five limitations bound the interpretation of these findings. First, pre-surgical cognitive status was assessed clinically rather than with the NEUROPSI, precluding true change-score analysis; the clinical assessment documented absence of gross pre-operative deficits in all 60 patients but cannot exclude subclinical impairment. Second, with 60 patients and event-per-variable ratios below 10, the study was adequately powered only for large effects; the null result for location is absence of evidence for large effects, not evidence of absence for moderate ones. Third, the one-month evaluation captures recovery from acute post-operative injury and cannot distinguish transient from persistent deficits. Fourth, radiotherapy and chemotherapy exposure at the time of assessment was not systematically recorded, limiting causal attribution to surgical injury alone. Fifth, the NEUROPSI brief battery assesses three cognitive domains; processing speed, IQ, and sustained attention—domains highly sensitive to tumor and treatment effects—were not evaluated, limiting comparability with the prospective international literature.

CONCLUSIONS

Tumor location did not predict neurocognitive deficit severity at one month after pediatric CNS tumor surgery in this exploratory cohort. Younger age predicted greater orientation impairment; no predictor emerged for selective attention or working memory. With deficits exceeding 40% across all three domains, these findings support routine early neuropsychological screening for every pediatric CNS tumor patient, regardless of lesion site. Prospective studies with standardized pre-surgical baselines, comprehensive neuropsychological batteries, longitudinal follow-up, and systematic recording of adjuvant treatment exposure are needed to determine whether these early deficits persist, resolve, or worsen over time.

Declarations

Competing Interests.

The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval.

This study was performed in line with the principles of the Declaration of Helsinki and NOM-012-SSA3-2012. Approval was granted by the Institutional Ethics Committee of CMN “20 de Noviembre,” ISSSTE (Registry RPI: 746.2023, approved December 26, 2023).

Consent to Participate.

Informed consent was obtained from all individual participants (or their parents/legal guardians) included in the study.

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Author Contribution

All authors contributed to the study conception and design. Data collection and neuropsychological assessment were performed by S.V. Nuñez-Pichardo, A. Benito-Resendiz, and D.N. Moya-Sánchez. Statistical analysis was conducted by S.V. Nuñez-Pichardo and R.L. Saldaña-González. The first draft of the manuscript was written by S.V. Nuñez-Pichardo and M.G. Ochoa-Madrigal, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

Figure 1. Patient selection and flow

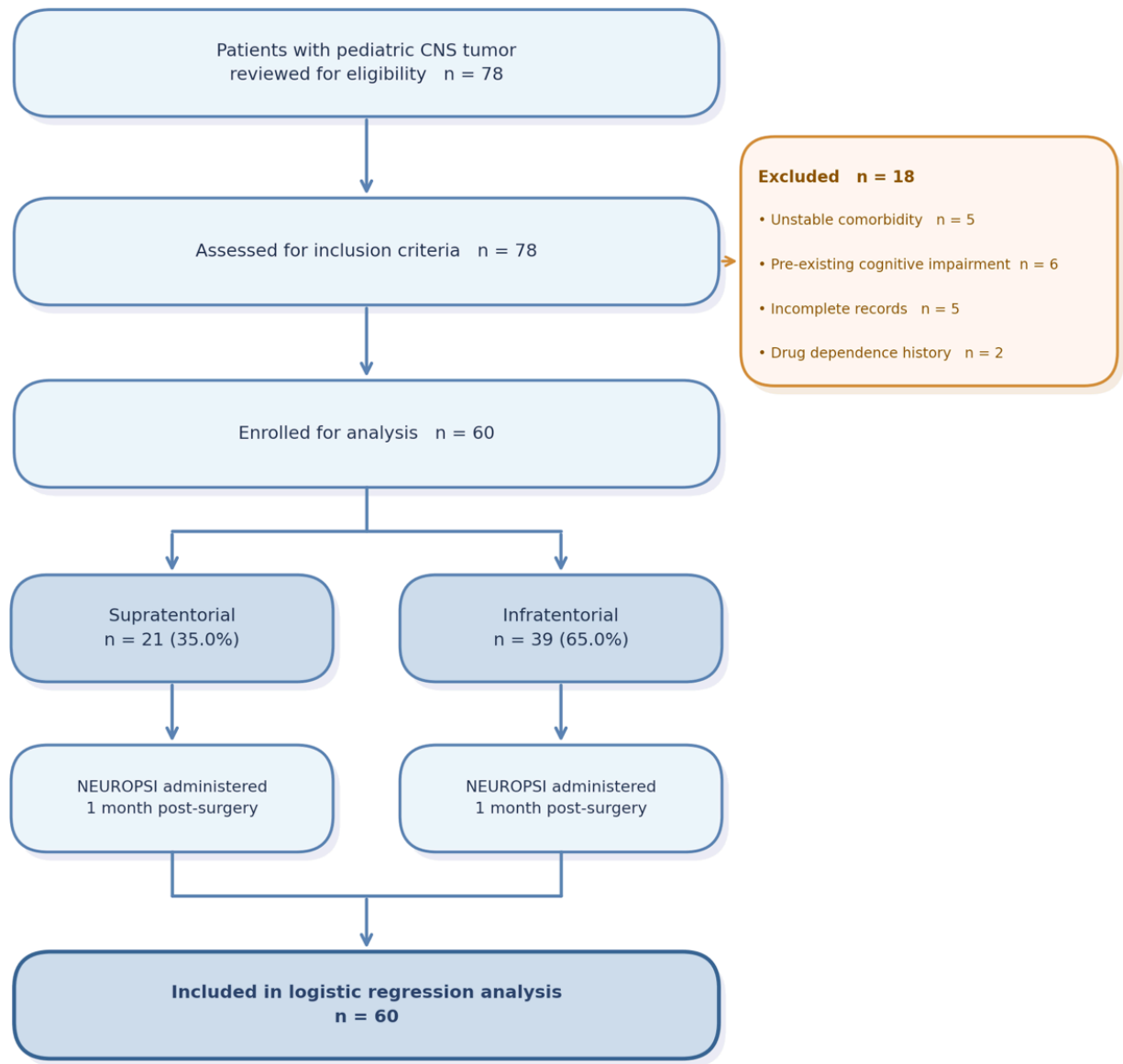
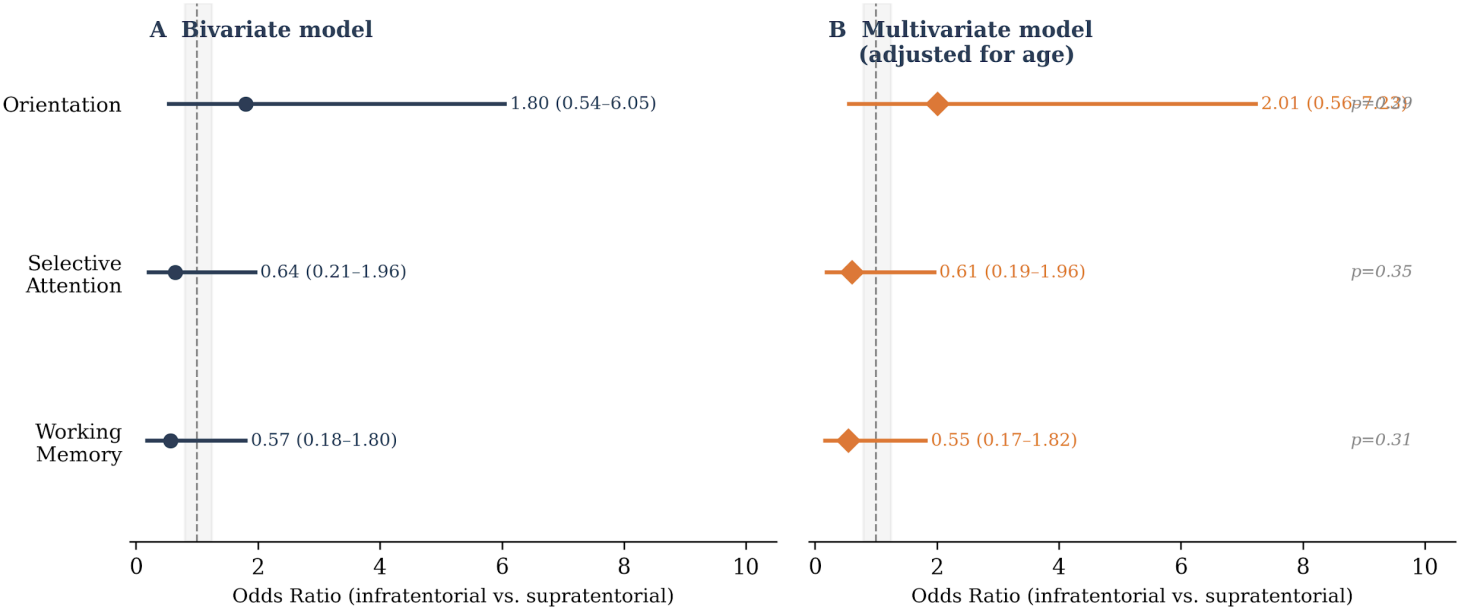


Figure 1

Of 78 patients assessed for eligibility, 18 were excluded by pre-specified criteria. The 60 enrolled patients were classified as supratentorial (n=21) or infratentorial (n=39) and evaluated with the NEUROPSI brief battery one month after surgery.

Figure 2. Effect of tumor location on neurocognitive deficit severity (infratentorial vs. supratentorial; reference OR = 1.0)

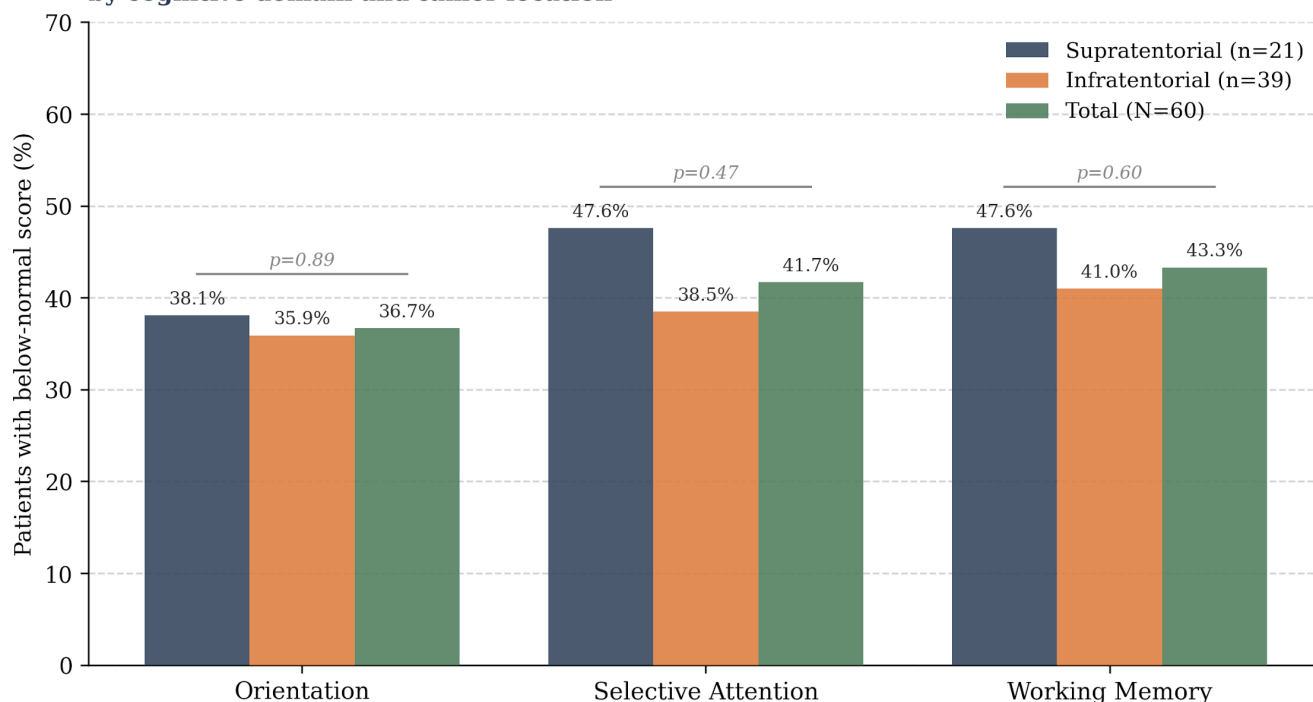


Diamonds = point estimate; horizontal lines = 95% CI. OR >1 indicates higher deficit odds with infratentorial tumors. All CI cross the null.

Figure 2

Forest plot of odds ratios (OR) for infratentorial versus supratentorial tumors across three cognitive domains. Panel A: bivariate models. Panel B: multivariate models adjusted for age. All 95% confidence intervals cross the null (OR=1.0, dashed line), indicating no statistically significant location effect. Circles = point estimates (bivariate); diamonds = point estimates (multivariate). CI = confidence interval.

Figure 3. Prevalence of neurocognitive deficits at one month post-surgery by cognitive domain and tumor location

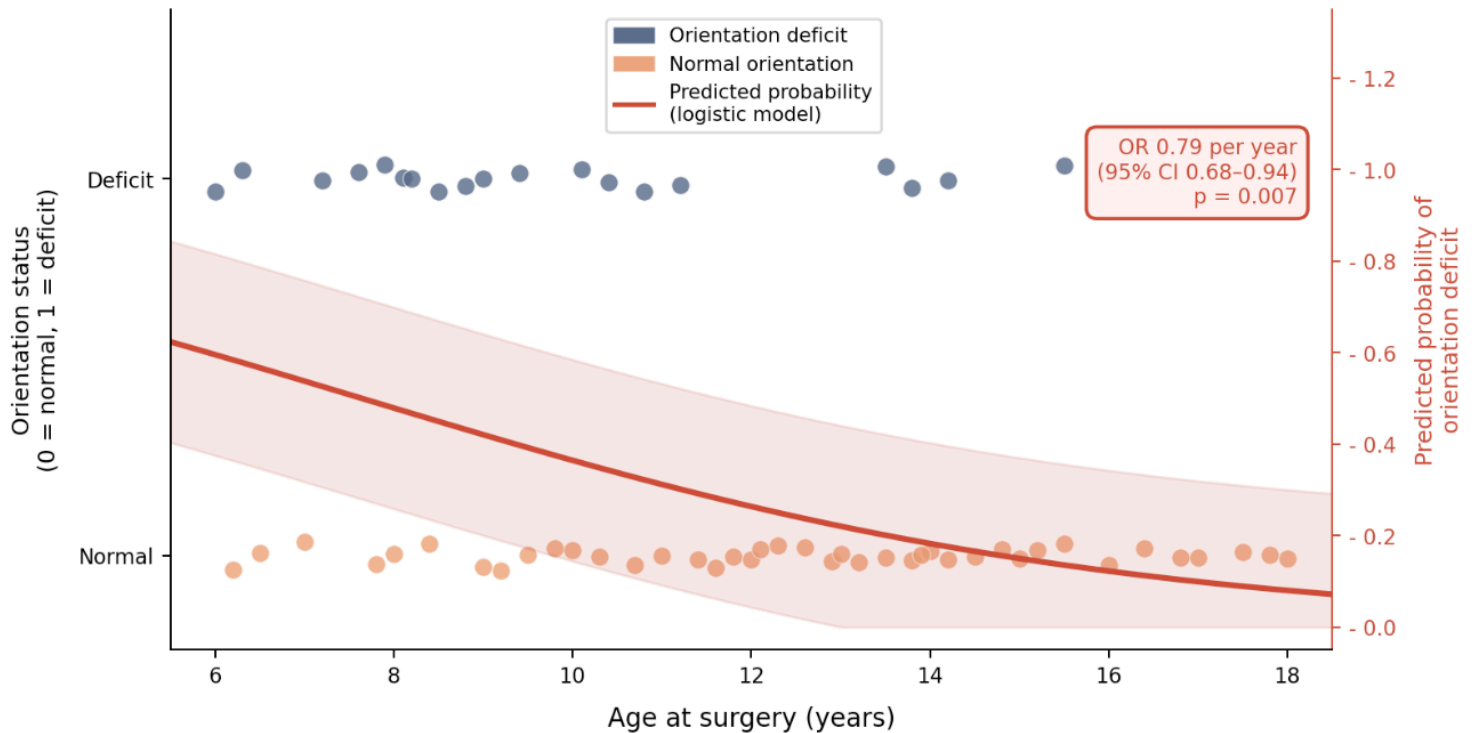


P values from Fisher exact test (location comparison). Percentages indicate proportion of patients scoring below the age-normed cut-off.

Figure 3

Percentage of patients scoring below the age-normed cut-off in each cognitive domain, stratified by tumor location and shown for the total cohort. P values from Fisher exact test comparing supratentorial vs. infratentorial groups. Deficit rates exceeded 40% for selective attention and working memory in both location groups.

Figure 4. Association between age and orientation deficit at one month after surgery (n = 60)



jitter added to binary outcome for visualization. Red curve = logistic regression predicted probability; shaded band = $\pm 22\%$ uncertainty envelope.

Figure 4

Binary outcome (0 = normal, 1 = below-normal orientation) plotted against age at surgery (jittered for visualization). The curve represents the logistic regression–predicted probability of orientation deficit as a function of age. Each additional year of age was associated with a 21% reduction in deficit odds (OR 0.79, 95% CI 0.68–0.94, $p=0.007$). The shaded band represents ± 1 SE around the predicted probability. CI = confidence interval; OR = odds ratio.

Supplementary Files

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