

Effects of Early Anesthesia Exposure on Cognition: Insights from the CHLA Retinoblastoma Program

Paula J. Belson, PhD, CRNA, FAANA,¹ Jesse L. Berry, MD,^{2,3} Nancy A. Pike, PhD, CPNP-PC/AC, FAAN⁴

¹Children's Hospital Los Angeles, ²USC Roski Eye Institute, Department of Ophthalmology, University of Southern California, ³Department of Ophthalmology, The Vision Center at Children's Hospital Los Angeles, ⁴Sue and Bill Gross School of Nursing, University of California, Irvine



Background

- Retinoblastoma (RB) is the most common intraocular malignancy of childhood.
- Treatment is extensive at a young age, requiring multiple eye examinations under general anesthesia.
- Previous studies on anesthesia exposure and neurodevelopment in children have found mixed results.
- Little is known how repeated exposure to anesthesia in early childhood affects cognitive function in RB survivors.

Purpose

- To compare cognitive function in adolescent and young adult (AYA) RB survivors compared to healthy controls and the association between anesthesia exposure and cognition in RB survivors.

Methods

- Cross-sectional study of a convenience sample of AYA RB survivors receiving follow-up care at CHLA
- Inclusion 14-26 years, speak and read English and exclusion for severe developmental delay, current diagnosis of second malignant neoplasm
- Healthy controls with no self-reported chronic medical or psychiatric conditions recruited from the Los Angeles community
- Instruments: Demographic data form; Hollingshead Socioeconomic Status measure; and the Montreal Cognitive Assessment (MoCA) (scores ≥ 26 , normal).
- Medical chart reviews were performed in the RB group to obtain clinical variables [laterality (unilateral versus bilateral) and anesthesia exposure (total number of anesthetics and inhalational anesthesia minutes)].
- Differences between groups were examined using two-sample t-test (continuous data) or Fisher's exact tests (categorical data). Spearman's rho (ρ) correlation was used to assess the association between anesthesia exposure and MoCA scores.

Results

- 98 RB survivors and 97 controls were recruited. In the RB group, 59% had unilateral disease and 41% had bilateral disease. RB patients were exposed to anesthesia 11 times (for 708 minutes) before age 3 on average (**Table 1**).
- RB patients scored significantly lower than healthy controls on several MoCA subscales, including Naming [effect size (ES)=-0.32, P=0.03], Attention (ES=-0.30, P=0.04), Language (ES=-0.40, P=0.005), and Abstraction (ES=-0.33, P=-0.02).
- Among all participants with available data (n=186), total childhood anesthesia exposure was negatively associated with MoCA total scores (ρ =-0.19, P=0.009; see **Figure 1**) and some subscale scores; however, when data from RB patients with known exposure before age 3 was examined (n=88), these associations were not observed (**Table 2**).

Table 1: Demographic Characteristics and MoCA scores of Retinoblastoma Survivors and Healthy Controls

Variables mean $\pm$ SD or n (%) [except where noted]	Retinoblastoma n=98	Control n=97	P Value
Age	17.56 $\pm$ 3.06	17.87 $\pm$ 2.82	0.47
Gender (Male)	48 (49%)	47 (48%)	1.00
Ethnicity			1.00
White	16 (16%)	16 (16%)	
Hispanic	63 (64%)	62 (64%)	
African American	4 (4%)	4 (4%)	
Asian	10 (10%)	11 (11%)	
Other	5 (5%)	4 (4%)	
SES (Hollingshead)	35.63 $\pm$ 14.35	39.86 $\pm$ 17.11	0.06
Public Insurance	59 (60%)	29 (30%)	<0.0001
Eye Involvement			—
Unilateral	58 (59%)	N/A	
Bilateral	40 (41%)		
Anesthesia Exposure			
Before Age 3			
N Exposures (range)	11.10 $\pm$ 9.44 (0-37)	N/A	—
Inhalation Time (minutes)	708 $\pm$ 574 (0-2399)	N/A	—
Total Childhood (Estimated)			
N Exposures (range)	17.69 $\pm$ 14.30 (0-63)	0.66 $\pm$ 1.17 (0-6)	<0.0001
Inhalation Time (minutes)	903 $\pm$ 721 (0-3603)	36.47 $\pm$ 64.49	<0.0001
MoCA Scores			
Total Score (range)	26.03 $\pm$ 2.43 (20-30)	26.84 $\pm$ 3.46 (4-30)	0.06
Visuospatial/Executive	4.12 $\pm$ 0.89 (n=91)	4.24 $\pm$ 0.90	0.38
Naming	2.93 $\pm$ 0.25 (n=91)	3.01 $\pm$ 0.23	0.03
Attention	5.43 $\pm$ 0.73	5.65 $\pm$ 0.72	0.04
Language	1.82 $\pm$ 0.97	2.19 $\pm$ 0.85	0.005
Abstraction	1.33 $\pm$ 0.70	1.55 $\pm$ 0.63	0.02
Delayed Recall	3.88 $\pm$ 1.08	4.00 $\pm$ 0.97	0.41
Orientation	5.91 $\pm$ 0.32	5.92 $\pm$ 0.31	0.84

SD = standard deviation; SES = socioeconomic status; MoCA = Montreal Cognitive Assessment

Figure 1. MoCA Total Scores vs. Total Childhood Anesthesia Exposure by Study Group

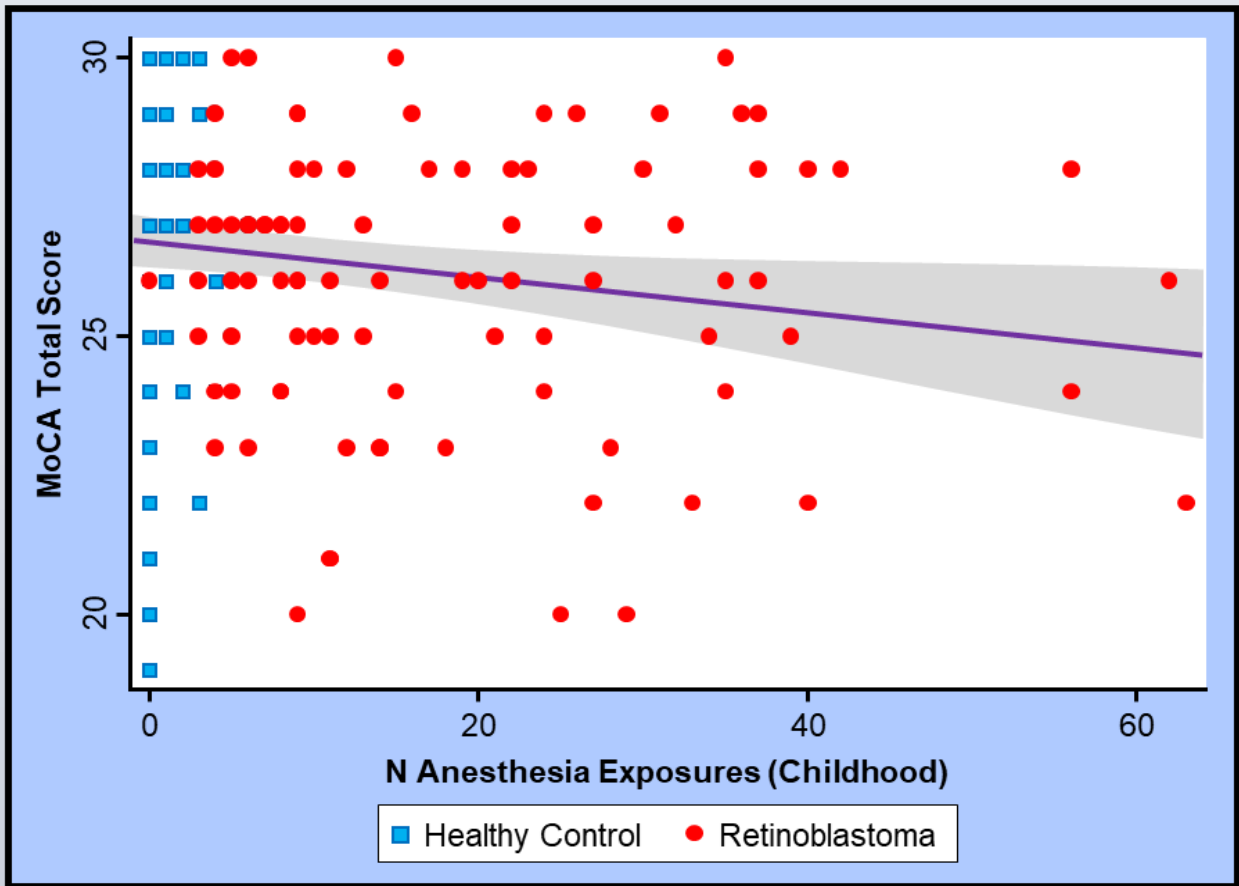


Table 2. Correlations between Total MoCA Scores and Anesthesia Exposure Before Age 3

Variables	Anesthesia Exposure			
	Total Childhood (n=186)		Before Age 3 (RB Only: n=88)	
MoCA Scores	Spearman's ρ	P Value	Spearman's ρ	P Value
Total Score	-0.19	0.009	-0.07	0.50
Visuospatial/Executive	-0.09	0.22	-0.11	0.32
Naming	-0.11	0.12	-0.01	0.92
Attention	-0.13	0.08	-0.04	0.72
Language	-0.15	0.04	-0.02	0.86
Abstraction	-0.16	0.03	0.03	0.80
Delayed Recall	-0.09	0.20	-0.06	0.61
Orientation	-0.02	0.78	-0.14	0.18

Results

- MoCA scores did not significantly differ between RB patients exposed to chemotherapy and those unexposed, or between unilateral versus bilateral RB.
- MoCA Total Scores were more strongly associated with SES (ρ =0.36, P<0.0001), with those who use public insurance (25.11 $\pm$ 3.53) scoring significantly lower than those who use private insurance (27.51 $\pm$ 1.92; ES=-0.80, P<0.0001).
- In a linear regression model with covariates, the number of anesthesia exposures before age three was significantly associated with total MoCA scores (β = -0.06, P=0.04) (**Table 3**).

Table 3. Linear Regression Model – Anesthesia Exposure Predicting MoCA Total Scores (RB Only, n=88)

Variables	β Coefficient	95% CI	P Value
N Exposures Before Age 3	-0.06	-0.12 – -0.003	0.04
Age	0.21	0.02 – 0.39	0.03
BCVA (visual acuity)	0.02	-1.41 – 1.45	0.98
Chemotherapy Used	-0.49	-1.57 – 0.59	0.38
Public Insurance	-1.64	-2.63 – -0.66	0.001
SES (Hollingshead)	0.05	0.01 – 0.08	0.005
Gender (Male)	0.36	-0.56 – 1.27	0.44
Constant	22.31	18.55 – 26.07	<0.0001

RB Patients exposed to inhalation anesthesia 11 times (average count) would be expected to score -0.66 points lower on MoCA (ES=-0.22).

Conclusion

- Anesthesia exposures before age 3, public insurance, and low SES were predictors of total MoCA scores in RB patients.
- Future studies are needed to explore anesthetic practices and ways to reduce the number of exposures to improve cognition in RB survivors.

Acknowledgements

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