Analysis Concept Form

STUDY TITLE: ADULT NEUROBEHAVIORAL LATE EFFECTS OF PEDIATRIC LOW GRADE BRAIN TUMORS

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BACKGROUND AND RATIONALE: Children are surviving brain tumors at increasing rates. The true legacy of childhood cancer spans the entire life, and so the importance of understanding the life trajectories of survivors cannot be over-estimated. *A better understanding of the degree and nature of the chronic/remote effects in these patients is critical in order to identify those at risk and to provide early interventions, as well as promote the development of less toxic treatments.* In the last 30 years, a substantial literature has developed attesting to the increased risk faced by these survivors. Most of this literature addresses the most aggressive/malignant tumors receiving multimodal, neurotoxic therapies (surgery, craniospinal radiotherapy, chemotherapy). Relatively little attention has been paid to low grade tumors receiving less toxic treatments (surgery alone or combined with focal radiotherapy). Indeed, it is often assumed that these tumors and treatments are associated with little to no long term effects (Pompili et al., 2002). Yet, several studies in recent years have called this assumption into question. Research conducted by the PI and associates has shown, for example, neurobehavioral morbidity of mild to moderate effect size in children following surgery for low grade astrocytoma. This literature, though, remains sparse and suffers from critical methodological limitations. The National Cancer Institute has identified late effects as a research priority so as to stimulate increased knowledge about the outcomes for these children—research that will better position the health care system to mitigate life-long debilitating consequences of cancer and its treatments. While late effects in children with low grade brain tumors may not be as severe as in higher grade tumors, low grade tumors comprise the highest incidence pediatric brain tumors, and so the net social burden represented by life-long accrued disability and under-employment may be substantial.

The proposed study makes use of an ongoing landmark epidemiologic investigation of childhood cancer (Childhood Cancer Survivor Study: CCSS) to identify adults who were treated (half with surgery only, and half with surgery plus focal radiotherapy) as children for low grade brain tumors. Their outcomes in critical neurobehavioral domains will be compared to those of age, gender, and education (of the family of origin) matched control participants in the CCSS. The proposed study promises to contribute important information about the adult outcomes of children treated for low grade brain tumors. *The strong sampling method, large sample size, inclusion of a control group, extensive outcome measurement guided by previous research, and developmental orientation redress many of the deficiencies in the existing research*. Being based in the CCSS, the proposed study benefits from the infrastructure and wealth of data that has been acquired by this study over the past 15 years-- information critical to identifying and recruiting diverse brain tumor and control groups. The extensive CCSS dataset also provides important health, demographic, and adult-adjustment data for statistical control and correlation with the detailed neurobehavioral and Socioeconomic Status (SES) outcome data acquired in the proposed study. Control for potential confounding effects will be achieved by equating the groups for some (e.g., gender, education of family of origin) while drawing from the extensive existing CCSS data set to statistically control for others (e.g. chronic medical conditions affecting overall health). In sum, we propose a comprehensive investigation that is (1) unique in the length of follow-up, (2) includes a healthy control group, and (3) applies an empirically-based outcome assessment strategy, that is (4) informed by developmental theory. By concentrating on patients treated for low grade tumors, we will be able to greatly

expand our knowledge of late-effects at the lower end of the gradient of treatment toxicity--i.e., those associated with tumors treated with surgery alone or in combination with focal radiotherapy.

SPECIFIC AIMS/OBJECTIVES/RESEARCH HYPOTHESES:

Specific Aim A. Ascertain the presence, degree, and nature of neuropsychological as well as SES effects in adults treated as children for low grade astrocytoma (LGA) as compared to healthy controls.

Hypothesis. A. 1: Participants with LGA will be impaired compared to Controls on measures of Composite Neuropsychological Functioning and Estimated IQ as well as SES as measured by Educational Attainment, Income, and Occupational Prestige

Hypothesis A. 2: Both the subgroup of LGA participants treated with surgery only (LGA-RT) and those treated with surgery plus focal radiotherapy (LGA+RT) will be impaired compared to Controls on measures of Composite Neuropsychological Functioning and Estimated IQ. as well as Socioeconomic Status (SES) as measured by Educational Attainment, Income, and Occupational Prestige

Specific Aim B. Within the LGA group, determine disease- and subject-related predictors of outcome

Hypothesis. B. 1: Degree of intellectual and neuropsychological impairment will correspond to tumor site, with cerebellar and cerebral hemisphere tumors associated with the least, and supratentorial midline and brainstem tumors the most impairment on Estimated IQ, Composite Neuropsychological Index, as well as SES as measured by Income, Educational Attainment, and Occupational Prestige

Hypothesis .B. 2: Compared to the LGA-RT subgroup, the LGA+RT subgroup will evince lower Composite Neuropsychological Functioning and Estimated IQ as well as SES as measured by Educational Attainment, Income, and Occupational Prestige

Hypothesis .B.3.: Compared to those treated at age 8 years and above, LGA patients treated at age 7 years and below will evince lower Composite Neuropsychological Functioning and Estimated IQ as well as SES as measured by Educational Attainment, Income, and Occupational Prestige.

Hypothesis B. 4: Composite Neuropsychological Functioning and Estimated IQ will correlate inversely with SES as measured by Educational Attainment, Income, and Occupational Prestige

Secondary Aims will explore: (A) Multivariate prediction models of outcome partitioning unique variance attributable to the predictors: treatment, tumor site, age at surgery, as well as an exploration of moderating variables such as Gender and Education of Family of Origin as a proxy measure of Cognitive Reserve. (B) The relationship between site of tumor and specific neuropsychological functions. (C) Accelerated cognitive aging using structural equation modeling. (D) The relationship between objective and subjective measures of neurobehavioral functioning.

ANALYSIS FRAMEWORK:

Primary Outcome Measures and Proposed Data Reduction Methods

With the large number of scores generated by the proposed outcome measures, data reduction methods were guided by empirical and theoretical considerations. For the Primary Outcome Measures, a composite score was derived (Composite Neuropsychological Index) that captures the diverse neuropsychological impact in a heterogeneous sample of survivors of brain tumors. Also, the inclusion of a measure of IQ (Estimated IQ) facilitates comparison of our findings with the extant literature where IQ is the most common outcome measure

used. The proposed battery also supports the other derived scores in the Secondary Analyses exploring more specific questions (i.e., the relationship between tumor site and various neuropsychological functions, accelerated cognitive aging, etc.).

Individual Tests and Estimated Time to Complete

TESTS (with Key Scores in parentheses)	**DESCRIPTION**	**JUSTIFICATION**	**TIME**
Intelligence: **WAIS-III** Vocabulary, Block Design, Digit Span, and Digit Symbol (Subtests Scores).	These subtests load highest on the four factors of Verbal Comprehension, Perceptual Organization, Working Memory, & Processing Speed	Selected subtests have been used in both brain tumor and aging research. They provide validated measures of working memory and processing speed as well as functions resilient to aging. *The Vocabulary and Block Design Subtests provide an Estimated IQ that Correlates .90 with WAIS Full Scale IQ (Clara & Huynh, 2003)*	30
Academic skills: **WRAT-IV** Reading and Arithmetic (Subtest Scores)	These subtests provide well-validated screening for word reading and math calculation skills	These basic skills are sensitive to anticipated differences in academic achievement between the brain tumor and control groups. Reading is also known to be resilient to aging.	15
Memory: **WMS-III** Logical Memory (I&II) and Visual Reproduction (I&II) (Subtest Scores)	These subtests assess recall of prose and geometric designs both immediately and after 25-35 minute delay	Tests of verbal and non-verbal memory provide important localizing information. In addition, initial encoding of information (measured on the immediate recall trials) is known to decline with age (Price, Said & Haaland, 2004)	20
Executive: **D-KEFS** Verbal Fluency Subtest (Letter Fluency Score), Design Fluency (Switching Score), Color-Word Interference (Switching Score), Trail-Making Subtests (Switching Score) **BRIEF*** —Adult Version (Behavioral Regulation & Metacognitive Indexes) *note, this is the Full 75 item Version, not the 15 item one used by Ellenberg et al.	The D-KEFS subtests selected constitute classic measures of response inhibition and mental flexibility. The BRIEF is a self-report inventory of various functional executive deficits experienced in daily life.	The executive functions of response inhibition and flexibility are particularly important in research on brain tumors (Berger et al, 2005) and aging as these appear to be particularly vulnerable. The BRIEF provides a unique way of assessing real-life manifestations of executive problems (See Ellenberg et al in Preliminary Studies section)	20
Fine motor: **Grooved Pegboard Test**—(Right and Left Hand Trials)	This peg-placement task is a sensitive measure of fine motor speed and dexterity.	Lateralized motor functioning provides important localizing information and can also be used to control for the effects of primary motor deficits	5
Attention/reaction time: **Conners' CPT-II** (Total Errors of Omission, Total Errors of Commission, Hit Reaction Time Scores)	A computer-administered visual vigilance task, the CPT measures attention and reaction time.	The CPT offers measures of several functions of importance to this study. It is known that errors of omission, commission, and reaction time change with age (Mani, Bedwell, & Miller, 2005; Conners, 2000).	15
Psychological adjustment: Brief Symptom Inventory-18 (BSI-18) (Depression, Anxiety & Somatization Factor Scores)	This is a standardized, self-report symptom inventory commonly used in research in medical settings. It has been demonstrated to have the same 3-factor structure (Depression, Anxiety, Somatization) as the 53 item BSI (Recklitis et al., 2006)	This will provide a measure of symptom intensity at the time of testing for statistical control. Since the BSI-18 was also administered in 2002 to CCSS participants (Zebrack, et al., 2004) it has the advantage of providing longitudinal ratings of psychological symptoms and thus classification of patients with chronic and acute adjustment problems.	5
Self-report cognitive functioning	The CFQ is a 25 item self-	The CFQ has been used in previous	5

Cognitive Failures Questionnaire (CFQ) (Total Score)	report scale that lists a variety of situations in everyday life where cognitive failures may occur	research on outcome after treatment for brain tumors where incremental validity over direct testing was demonstrated (Waber et al, 2006)	

Composite indexes as Primary Outcome Measures. (see Appendix A)

COMPOSITE NEUROPSYCHOLOGICAL INDEX (CNI) (Hypotheses A.1, A.2, B.1, B.2, B.3, B.4) will be derived by averaging the z-scores for all of the Key Scores specified above in Table D. 4.6 (not including the inventories) converted to IQ-scale.

ESTIMATED IQ (EIQ) (Hypotheses A.1, A.2, B.1, B.2, B.3, B.4) comprised of the mean of the Vocabulary and Block Design subtests of the WAIS-III, converted to IQ-scale (mean=100, sd=15).

Composite and domain indexes/scores used in Secondary Analyses. (see Appendix A)

COMPOSITE AGING INDEX (CAI) comprised of the average z-scores for WAIS-III Digit Symbol, Switching Trial from the D-KEFS Trails subtest, and the Switching Trial of the D-KEFS Color-Word Interference subtest. These tests were selected because they include measures of processing speed and other "fluid" abilities, have empirically-established sensitivity to aging-effects, and are among the earliest to decline. Normative data on these measures indicate raw score declines of .66-.75 of a standard deviation across the age span sampled in this study.

COMPOSITE RESILIENCE INDEX (CRI) comprised of the average z-scores for Vocabulary, Reading, and Letter Fluency converted to IQ-scale. In attempting to demonstrate changes associated with aging, it is important to contrast such measures (Composite Aging Index) with those known to be relatively resilient to change with aging. The tests comprising the Composite Resilience Index are prototypic measures of these "crystallized" abilities. Normative data on these measures indicate raw score stability or even gains across the age span sampled in this study.

VERBAL DOMAIN SCORE comprised of the average z-scores for the WAIS-III Vocabulary, WRAT-IV Reading, and D-KEFS Verbal Fluency subtests.

VISUAL-SPATIAL DOMAIN SCORE comprised of the average z-scores for the Block Design and Design Fluency subtests.

MEMORY DOMAIN SCORE comprised of the average z-scores for the Logical Memory I &II, and Visual Reproduction I & II subtests.

ATTENTION/PROCESSING SPEED DOMAIN SCORE comprised of the average z-scores for the Digit Span, Digit Symbol, CPT omissions, CPT commissions scores.

MOTOR DOMAIN SCORE comprised of the average z-scores for the Right and Left Hand Trials of the Grooved Pegboard Test.

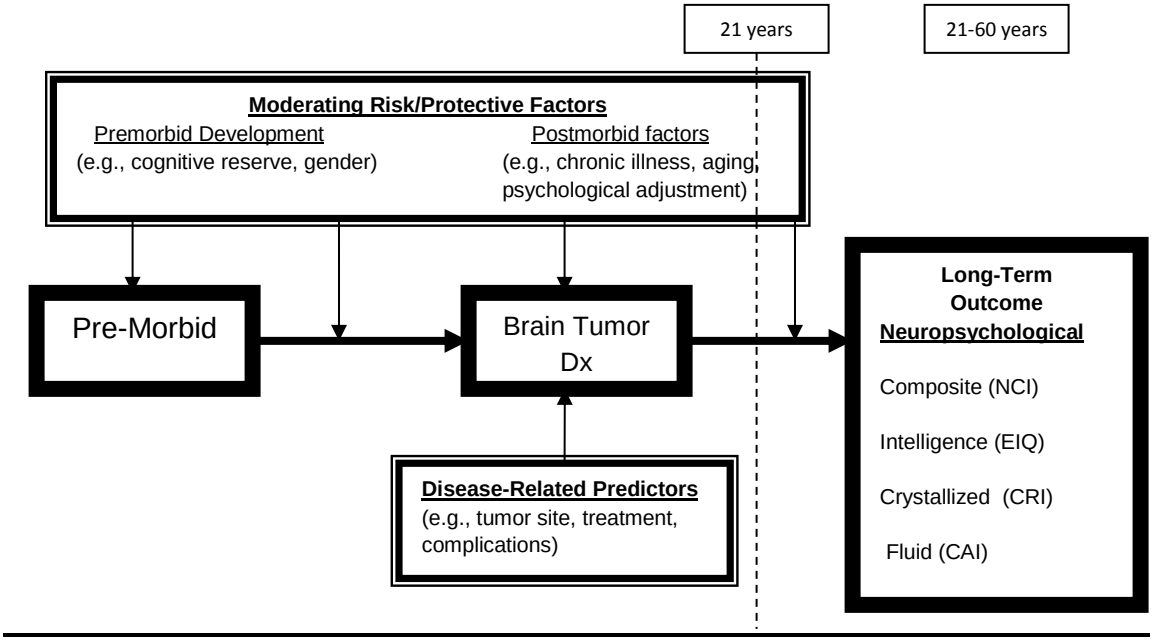
EXECUTIVE DOMAIN SCORE comprised of the average z-scores for the Verbal Fluency Switching score, Design Fluency Switching score, Color-Word Switching score, and Trails Switching score.

Since we are proposing homogeneous constructs for the CAI, CRI, and all of the Domain Scores, these indices will be checked for internal consistency with coefficient alpha greater than or equal to .60. Under circumstances in which this is not met, the component that correlates least with the others will be removed

from the composite until this requirement is met. Composites, rather than individual test scores, are proposed because they are known to be more reliable. However, it is recognized that with the use of composite scores comes the risk of obscuring more specific effects on individual measures. Whenever significant results are found with the composite scores, secondary analyses will explore any such relationships in the data. We also propose to use standard scores rather than raw scores in the analyses. One could argue that raw scores would have more variance and therefore would be more sensitive to group differences. However, because of test scaling differences, the use of composites would not be possible without conversion to a common metric. Again, we plan to explore in our secondary analyses raw scores relationships on select measures that may have been attenuated by conversion to standardized scores.

Conceptual Model

Biopsychosocial life-span development research benefits from the recursive calibrating of data with theory, and so the model presented below provides a context for our investigation of remote late-effects, placing it in temporal space. The proposed study is not meant to provide an exhaustive investigation of all of the factors represented below that potentially contribute to outcome. Rather, we present this diagram to further illustrate the conceptual orientation from which the specific hypotheses in this application derive.



Covariate preprocessing and selection

CANDIDATE COVARIATES	Source
Chronic medical conditions (e.g., diabetes)	CCSS
Medications potentially affecting cognition/behavior	Current study
Psychiatric symptoms (e.g., anxiety, depression)	Current study
Vision ,hearing or motor deficit	Current study
Other neurologic condition/injury (e.g., epilepsy)	Current study
Hx of tumor recurrence	CCSS
Extent of resection	Current study
Size of tumor	Current study
Perisurgical complications	Current study
Chemotherapy	CCSS
Dx of NF-1	CCSS
*Gender	Current study
*Education of family of origin	Current study
(*matching variables in the between group analyses)	

The models proposed in the next section (Primary and Secondary Analyses) will adjust for covariates from among this list of candidate covariates that, following backward elimination and forward inclusion stepwise multiple regression analyses, are found to be independently related to the relevant outcome measure (dependent variable) at $p \leq .10$ or if their inclusion proves important in modifying the effect of the risk factor of interest. In regards to *chemotherapy*, the CCSS has developed a conversion of alkylating agentes to a cyclophosphamide equivalent dose (CED) exposure that will be used, along with total anthracycline dose. In regards to a diagnosis of *Neurofibromatosis Type 1 (NF-1)*, from the CCSS dataset we estimate that only 4% of the LGA sample will have this diagnosis, but because of the known neurobehavioral risks associated with this condition, we will statistically control for these effects.

Proposed Statistical Analyses Addressing Each Hypothesis

Proposed analyses for hypotheses A.1, A.2. : For these hypotheses, the impact of the specified risk factor on the outcome measures listed for that hypothesis will be evaluated using multivariate methods for comparing multiple outcome measures between groups. MANOVA models will be tested for the two sets (neuropsychological, SES) of outcome measures (with appropriate covariates included) as overall omnibus tests to control Type 1 error. If the overall F test is significant, the omnibus MANOVAs will be followed up by individual adjusted post-hoc tests for each outcome variable separately. For Hypothesis A.1 and A.2, the control group may include some siblings of the tumor survivor group, which could theoretically impose some intra-family correlation on the structure of our data, thereby raising concerns about the assumption of independent observations required by the proposed analyses. However, we expect the impact of this correlation to be minimal as the tumor survivors' siblings account for only 85 of the 4,000 subjects in the CCSS sibling population, from which pool we will be sampling only about 100 controls. Based on these numbers and the random selection process, we would expect to select only 2-3 siblings of tumor survivors [(85/4000)×100 = 2.215]. We will evaluate the number of sibling pairs included in the final sample and if expected to impact results, make appropriate adjustments to the analysis to account for intra-family correlation (such as use of generalized estimating equation approaches or mixed models for reported univariate results). All analyses will be carried out with two-sided α levels of 0.05, with care taken to place all statements of significance in the context of the number of independent statistical comparisons that were carried out.

Proposed analyses for hypotheses B.1, B.2, B3.: For Hypothesis B.1, B.2, and B3, MANOVA and subsequent single outcome models, similar to those planned for Hypothesis A.1 and A.2 will be carried out. For Hypothesis B.4, correlations between the neuropsychological and SES measures will be evaluated using partial Pearson correlation (appropriate covariates partialled). As a control, participant age will be entered into these models since Education, Income and Occupational Prestige will most likely increase as a function of age.

Integrative table of hypotheses, risk factors, outcomes and analyses

Hypothesis	Risk Factors (Independent Variable)	Outcomes (Dependent Variable)	Analyses
A.1 Participants with LGA will be impaired compared to Controls on measures of Composite Neuropsychological Functioning and Estimated IQ as well as Socioeconomic Status (SES) as measured by Educational Attainment, Income, and Occupational Prestige	Controls vs. LGA	EIQ, NCI, Income, Education, Occupation	Omnibus MANOVA Followed by single outcome comparisons
A.2. Both the LGA-RT, and LGA+RT subgroups will be impaired compared to Controls on measures of Composite Neuropsychological Functioning and Estimated IQ. as well as Socioeconomic Status (SES) as measured by Educational Attainment, Income, and Occupational Prestige	Controls vs. LGA+RT and Controls vs LGA-RT	EIQ, NCI, Income, Education, Occupation	Omnibus MANOVAs Followed by single outcome comparisons
B.1. Degree of intellectual neuropsychological impairment and SES will correspond to tumor site, with cerebellar and cerebral hemisphere tumors associated with the least, and supratentorial midline and brainstem tumors the most impairment.	cerebellar and cerebral hemisphere vs supratentorial midline and brainstem sites	EIQ, NCI, Income, Education, Occupation	Omnibus MANOVA Followed by single outcome comparisons
B.2: Compared to LGA-RT, LGA+RT will evince lower Composite Neuropsychological Functioning and Estimated IQ as well as Socioeconomic Status (SES) as measured by Educational Attainment, Income, and Occupational Prestige	LGA+RT vs LGA-RT	EIQ, NCI, Income, Education, Occupation	Omnibus MANOVA Followed by single outcome comparisons
B.3: Compared to those treated after age 8, LGA patients treated before age 8 years will evince lower Composite Neuropsychological Functioning and Estimated IQ as well as Socioeconomic Status (SES) as measured by Educational Attainment, Income, and Occupational Prestige.	Ages at treatment: <8, >8	EIQ, NCI, Income, Education, Occupation	Omnibus MANOVA Followed by single outcome comparisons
B.4. Composite Neuropsychological Functioning and Estimated IQ will correlate inversely with SES as measured by Educational Attainment, Income, and Occupational Prestige	EIQ, NCI	Income, Education, Occupation	Partial Pearson r With covariate correction

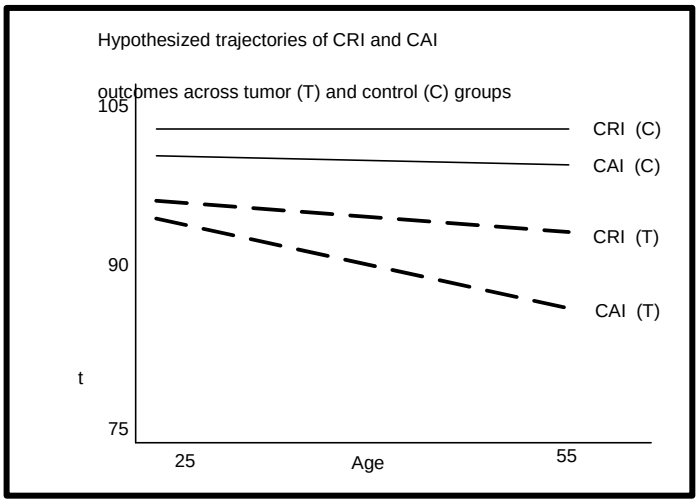
Secondary Analyses

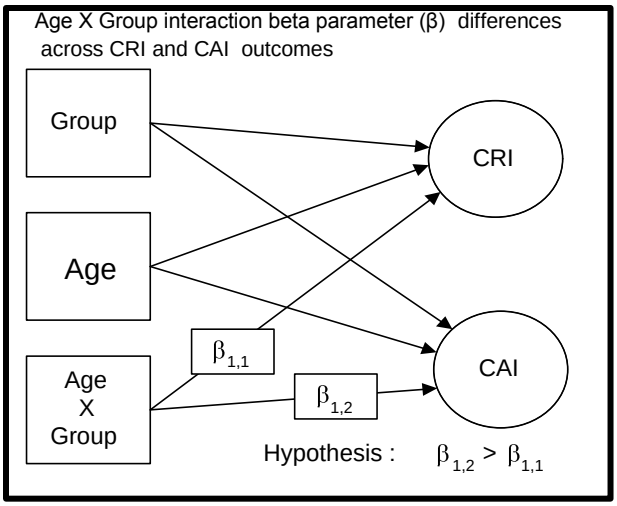
Five sets of Secondary Analyses are planned:

Disease Predictor Variables	Moderator Variables	Confounding Variables
Treatment (-RT, +RT)	Age at treatment	Medications
Tumor size	Gender	Psychological symptoms
Tumor site	Education of Family of Origin	Neurosensory deficits (vision & hearing)
Extent of resection		
Complications		
Tumor recurrence		

(A) Multiple Regression Analyses will extend the investigation of outcome as it relates to disease predictor, moderator, and confounding variables through multivariate modeling partitioning unique variance attributable to these variables. While these three categories are not conceptually-distinct, for the purposes of clarity, they are grouped as above.

(B) Structural Equation Modeling as an initial exploration of accelerated cognitive aging for some (Cognitive Aging Index) but not other (Cognitive Resilience Index) functions (see model below). Under this revised application, power to explore accelerated cognitive aging is greatly improved by the increase in sample size, increased effect size with the inclusion of patients treated with RT, and a sharpening of the CRI and CAI constructs such that they are purer measures of resilience and aging.





(C) The relationship between site of tumor (along axial, coronal, and saggital planes) and specific neuropsychological functions by Domains.

(D) The relationship between anatomic segment(s) irradiated and neuropsychological functions by Domains.

(E) The relationship between objective (standardized tests) and subjective (BRIEF-A and CFQ) measures of neurobehavioral functioning.

Several additional exploratory analyses are planned. First, the plan for combining test scores into composite variables defined above exemplifies a good *a priori* approach to proposing testable hypotheses. However, from an empirical standpoint, this may not turn out to be the optimal way of combining these variables. We therefore plan to subject the various scores generated by this battery to a Principal Components Factor Analysis followed by an additional set of analyses using the resultant factor scores as dependent variables. Second, we will also explore the sensitivity of raw scores to the effects hypothesized. Third, the relationships between measures of emotional adjustment (derived from the current study as well as the CCSS dataset) and neuropsychological variables will be explored.

SPECIAL CONSIDERATIONS:

1. Final sample sizes will be somewhat smaller than originally proposed. It is anticipated that by the end of the funding period (April 31st , 2014) there will be about the number of subjects listed below in each of the three groups (LGA-RT, LGA+RT, Control) with complete test data (full assessments) and with questionnaires only.
   Totals for full assessment: 291
   LGA-RT = 87
   LGA+RT = 98
   Control = 106
   Totals for Questionnaires Only = 75 (35 LGA-RT, 40 LGA+RT)
2. Because of #1, it will be important to establish the degree to which the final sample is representative of the overall eligible pool from the CCSS. These analyses are not described above.

3. Not all of the Candidate Covariates will be used in the final analyses because of limited information that could be gleaned from the medical record (e.g., extent of resection, perisurgical complications).
4. As per #1 In addition to the sample of approximately 291 with complete test data as described above, there are an additional 75 subjects who participated via mail by completing two of the questionnaire measures (BRIEF, BSI-18). Data from these subjects will be included in analyses of specific measures (Secondary and Exploratory Analyses). It will be important to determine the degree to which these 75 subjects are similar to the LGA subjects who completed full assessments.

Appendix A: Composite Score Derivations

Composite Score	Step 1:Individual Scores comprising composites	Step 2: Transform each to IQ Scale	Step 3: Composite Mean Score	Step 4: Composite Construct Score
Composite Neuropsychological Index (CNI)	Scaled Scores (SS) from the following tests: Block Design, Digit Span, Coding, Vocabulary, Logical Memory I, Logical Memory II, Visual Reproduction I, Visual Reproduction II, Trail Making Test Number-Letter Switch, Color Word Inhib/Switch, Verbal Fluency Test Letter Fluency, Design Fluency Switch.	[[(SS-10)/3] X 15] +100	Arithmetic mean of all scores will be the final CNI	No Composite Construct Score
	Standard Scores from the following tests: WRAT Read, WRAT Math, Grooved Pegs Dom, Grooved Pegs Non-Dom	(no need to transform since already in IQ scale)		
	T Scores from the following tests: CPT Omission, CPT Commission, CPT Hit Reaction Time **(19 scores)**	[[(T-50)/10] X (-15)] + 100 (Multiplying by negative 15 maintains consistency with other scores in which high scores indicate high ability)		
Estimated IQ (EIQ)	Scaled Scores (SS) from: Vocabulary and Block Design. **(2 scores)**	[[(SS-10)/3] X 15] +100	Arithmetic mean	No Composite Construct Score
Composite Aging Index (CAI)	Scaled Scores from: Coding, Trail Making Test Number-Letter Switch, Color Word Inhib/ Switch **(3 scores)**	[[(SS-10)/3] X 15] +100	Arithmetic mean	Internal consistency with Coefficient Alpha: Retain all scores if at least .60. If less, eliminate score correlating lowest with other scores. Repeat as necessary until Coefficient Alpha equals or exceeds .60. Then calculate mean of remaining scores to arrive at the Composite Construct Score
Composite Resilience Index (CRI)	Scaled Scores from: Vocabulary, Reading, Letter Fluency **(3 scores)**	[[(SS-10)/3] X 15] +100	Arithmetic mean	Internal consistency with Coefficient Alpha: Retain all scores if at least .60. If less, eliminate score correlating lowest with other scores. Repeat as necessary until Coefficient Alpha equals or exceeds .60. Then

				calculate mean of remaining scores to arrive at the Composite Construct Score
Verbal Domain	Scaled Scores from: Vocabulary, WRAT Reading, Letter Fluency. **(3 scores)**	[[(SS-10)/3] X 15] +100	Arithmetic mean	Internal consistency with Coefficient Alpha: Retain all scores if at least .60. If less, eliminate score correlating lowest with other scores. Repeat as necessary until Coefficient Alpha equals or exceeds .60. Then calculate mean of remaining scores to arrive at the Composite Factor Score
Visual-Spatial Domain	Scaled Scores from: Block Design, Design Fluency **(2 scores)**	[[(SS-10)/3] X 15] +100	Arithmetic mean	Internal consistency with Coefficient Alpha: Retain all scores if at least .60. If less, eliminate score correlating lowest with other scores. Repeat as necessary until Coefficient Alpha equals or exceeds .60. Then calculate mean of remaining scores to arrive at the Composite Construct Score
Memory Domain	Scaled Scores from: Logical Memory I, Logical Memory II, Visual Reproduction I, Visual Reproduction II **(4 scores)**	[[(SS-10)/3] X 15] +100	Arithmetic mean	Internal consistency with Coefficient Alpha: Retain all scores if at least .60. If less, eliminate score correlating lowest with other scores. Repeat as necessary until Coefficient Alpha equals or exceeds .60. Then calculate mean of remaining scores to arrive at the Composite Construct Score
Attention/Processing Speed Domain	Scaled Scores from: Coding, Digit Span CPT Omissions, CPT Commissions **(4 scores)**	[[(SS-10)/3] X 15] +100 [[(T-50)/10] X (-15)] + 100	Arithmetic mean	Internal consistency with Coefficient Alpha: Retain all scores if at least .60. If less, eliminate score correlating lowest with other scores. Repeat as necessary until Coefficient Alpha equals or exceeds .60. Then calculate mean of remaining scores to arrive at the Composite Construct Score
Motor Domain	Standard Scores for: Grooved Pegs Dom, Grooved Pegs Non-Dom **(2 scores)**	(no need to transform since already in IQ scale)	Arithmetic mean	Internal consistency with Coefficient Alpha: Retain all scores if at least .60. If less, eliminate score correlating lowest with other scores. Repeat as necessary until Coefficient Alpha equals or exceeds .60. Then calculate mean of remaining scores to arrive at the Composite Construct Score
Executive Domain	Standard Scores for:	[[(SS-10)/3] X 15]	Arithmetic mean	Internal consistency with

	Verbal Fluency Test Letter Fluency, Design Fluency Switch, Color Word Inhib/Switch, Trail Making Test Number Letter Switch **(4 scores)**	+100		Coefficient Alpha: Retain all scores if at least .60. If less, eliminate score correlating lowest with other scores. Repeat as necessary until Coefficient Alpha equals or exceeds .60. Then calculate mean of remaining scores to arrive at the Composite Construct Score