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NCOG-71. GENOME ASSOCIATIONS WITH NEUROCOGNITIVE OUTCOMES, CEREBRAL MICROBLEEDS (CMBS), AND BRAIN VOLUME AND WHITE MATTER (WM) CHANGES IN PEDIATRIC BRAIN TUMOR SURVIVORS

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III: >12 cycles). RESULTS: We observed that STR was beneficial for females (HR=0.52; CI=0.33-0.83; p-value=0.013), while for males the benefit was not detected (HR=0.73; CI=0.46-1.15; p-value=0.173) for STR but was detectable for GTR (HR=0.58, CI=0.37-0.90; p-value=0.014). Females receiving 7-11 cycles of TMZ showed a survival benefit (HR=0.52; CI=0.12-0.53; p-value=0.048) while males in the same group did not (HR=0.74; CI=0.46-1.19; p-value=0.21), in comparison to those in group I of TMZ cycles. No sex differences were identified in patients receiving < =6 cycles or >=12 cycles. CONCLUSION: Together, our results contribute to the growing literature that sex differences exist in GBM patients, even in response to standard-of-care therapies. This should be accounted for when designing clinical trials for GBM so that we may advance our pursuit to deliver personalized medicine.

NCOG-70. RELIABILITY AND VALIDITY OF A NEW SELF-REPORT INDEX OF COGNITIVE CONCERNS IN BRAIN TUMOR PATIENTS

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INTRODUCTION: Subjective cognitive dysfunction is an important outcome measure in neuro-oncology and may provide additional information beyond performance-based neuropsychological testing. The Functional Assessment of Cancer Therapy-Brain (FACT-Br) is a frequently used quality of life (QoL) measure that includes indices of physical, emotional, social, and neurologic aspects of disease, but does not measure cognitive concerns. This study seeks to develop and validate an index of self-reported cognition derived from existing items on the FACT-Br. METHODS: 145 patients (*Mage*=51.08, *Medu*=15.63) with heterogeneous brain tumor diagnoses completed neuropsychological evaluation including cognitive testing and self-report measures. Nine FACT-Br items regarding cognition were combined to form the Cognitive Index (CI). Reliability of the CI was measured with Cronbach's alpha. Concurrent validity was assessed by correlating the CI with the Patient-Reported Outcomes Measurement Information System (PROMIS) Cognitive Abilities-8 or PROMIS Cognitive Concerns-8. Discriminant validity was assessed by correlation of the CI with other FACT-Br indices and the Beck Depression and Anxiety Inventories (BDI, BAI). RESULTS: Internal consistency within the CI was high (Cronbach's a 0.864). The CI correlated strongly with the PROMIS-Abilities (r =.680; p< 0.001) and PROMIS-Concerns (r=.780; p< 0.001) indicating high convergent validity. Moderate correlations were observed between the CI and the physical and functional subscales of the FACT (r=.453 and .555), whereas correlations with the social and emotional functioning subscales were weaker (r=.381 and .325). The FACT-Br-CI correlated strongly with BDI (r=-.622) and more weakly with the BAI (r=-.344). Consistent with prior literature, the CI showed modest correlations with neuropsychological measures, including verbal memory encoding (r=.300), verbal fluency (r=.252) and a composite measure of cognition (r=.249; all p's< .01). CONCLUSIONS: The FACT-Br-CI is a reliable and valid measure of self-reported cognition. Studies that include the FACT-Br could be retrospectively analyzed to assess self-reported cognitive outcomes, enriching the information gained from prior research.

NCOG-71. GENOME ASSOCIATIONS WITH NEUROCOGNITIVE OUTCOMES, CEREBRAL MICROBLEEDS (CMBS), AND BRAIN VOLUME AND WHITE MATTER (WM) CHANGES IN PEDIATRIC BRAIN TUMOR SURVIVORS

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OBJECTIVE: To identify genetic predictors of neurocognition, CMBs, brain volume, and WM changes in pediatric brain tumor survivors. METHODS: Patients were selected from an existing cohort (RadART) if they had: 1) at least one neurocognitive evaluation using computer-based CogState; 2) available DNA; 3) standard imaging. Candidate gene or genome-wide genotyping was performed on all patients. CMBs were identified using a semi-automated algorithm developed in MATLAB. Volume of T2/FLAIR WM signal abnormality was measured using a semi-automated method based on a convolutional neural network. Brain volume and cortical thickness were measured using FreeSurfer volumetric analysis. Logistic and linear regression were done to compare phenotypes with candidate genotypes. Genome-wide efficient mixed-model analysis was done to compare neurocognition and CMBs. Gene set analysis was done using https://fuma.ctglab.nl/. RESULTS: APOE4 was a candidate variant associated with non-lobar, larger volume CMBs (p< 0.05). At the GWAS-level (n=225), specific genes trended with visual memory, psychomotor function, and CMB count (p< $5x10^{-8}$). Using gene set analyses, there were gene set trends seen with CMB count and psychomotor function. Small sample size and low mutant allele frequency limited reliability of these findings. Preliminary volumetric analysis show reduced volume within the right parietal, medial occipital and inferior temporal lobes with increased cortical thickness in the left occipital and medial parietal lobe in patients carrying the ApoE4 allele. WM signal assessments are ongoing. CONCLUSION: Genetic markers may be associated with neurocognition, CMBs, brain volume and WM changes in pediatric brain tumor survivors; however, larger cohorts are needed to confirm specific gene relevance.

NCOG-72. DIFFERENTIAL EFFECTS OF SURGERY AND CHEMOTHERAPY ON CHILDREN WITH POSTERIOR FOSSA BRAIN TUMORS

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BACKGROUND: Few neuroimaging studies of children with brain tumors treated with chemotherapy without radiation exist, and the neuropsychological effects of chemotherapy remain unclear. We aimed to differentiate the effects of surgery and chemotherapy on brain microstructure and cognition. METHODS: Twenty-eight children with a history of posterior fossa tumor (17 treated with surgery alone; 11 treated with surgery + chemotherapy), and 21 sibling controls (n= 49) underwent diffusion tensor imaging (DTI) and neuropsychological assessment a mean of 4.5 (surgery group) to 9 years (surgery + chemotherapy group) after treatment. Psychometric measures focused on general intelligence, executive functions, processing speed, learning and memory, and social-emotional functioning. Age at diagnosis and time since diagnosis were covariates in the analyses. Group differences in DTI findings and psychometric scores, and correlations between psychometric scores and DTI results were examined. RESULTS: Mean fractional anisotropy (FA) in the prefrontal cortex, white matter tracts, hippocampus, putamen, globus pallidus, thalamus, and pons were significantly (z≥ 2SD) lower in children treated with surgery + chemotherapy compared to those treated with surgery alone. In neuropsychological evaluation, the patient groups differed only in receptive vocabulary (p= 0.05), with children treated with surgery + chemotherapy scoring lower. Both patient groups scored lower than healthy sibling controls on measures of visuoconstructional reasoning (p= 0.02) and delayed visual (p= 0.02) and spatial memory (p= 0.01). Lower FA in the uncinate fasciculus and higher FA in the right thalamus associated with higher scores on general intelligence (p= 0.003, p= 0.002), and higher FA in the right thalamus associated with higher scores on spatial learning (p= 0.01) and memory (p= 0.01) in children treated with surgery + chemotherapy. CONCLUSIONS: Chemotherapy is associated with injury to the microstructure of white and gray matter and neuropsychological deficits not seen in children with posterior fossa tumors treated with surgery alone.

NCOG-73. EFFECT OF TIME TO DIAGNOSIS IN CHILDREN WITH MALIGNANT CENTRAL NERVOUS SYSTEM TUMORS ON SURVIVAL OUTCOMES AND DISEASE-ASSOCIATED MORBIDITY: AN INSTITUTIONAL COHORT STUDY

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OBJECTIVE: To determine the impact of time to diagnosis on disease related morbidity and mortality. METHODS: This is a retrospective