assess functioning. Raw scores were standardized for comparison against age- and (where appropriate) gender-matched peers. **Results:** In addition to her medical diagnoses of RSTS, Type 2, and her prior diagnosis of ADHD – Combined Subtype, LX also met diagnostic criteria for Specific Learning Disability with Impairment in Reading and a Mixed Receptive-Expressive Language Disorder. LX also met criteria for Encephalopathy as characterized by weakness in visual perception, visuospatial judgment and reasoning, and working memory. LX demonstrated adaptive functioning weaknesses in domains such as self-direction, and self-care, while communication skills were reported to be average. Overall, LX's current levels of general cognitive ability and adaptive functioning were consistent with Borderline Intellectual Functioning; however, the diagnosis was deferred at present. Parents and teachers reported difficulties with peer relationships, hyperactivity, and aggression, consistent with known features of this condition. Strengths were noted in verbal and nonverbal reasoning, spelling, math calculation, verbal and visual memory, and improvement in attention with medication, which all fell within the broadly average range of functioning. **Conclusions:** LX's presentation and pattern of neuropsychological findings are consistent with the current conceptualization of development in RSTS, Type 2, but reflect a more nuanced clinical picture. In particular, although general cognitive ability was borderline overall, deficits were largely circumscribed to spatial reasoning, with broadly average verbal and nonverbal reasoning abilities. This case highlights the importance of comprehensive neuropsychological testing of patients with RSTS. Reporting of general cognitive ability scores alone may obscure underlying patterns of relative strengths and weaknesses that have important ramifications for both targeted interventions and for a more positive prognosis related to functioning in academic, home, and community environments.

Categories: Genetics/Genetic Disorders
Keyword 1: neuropsychological assessment
Keyword 2: cognitive functioning
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56 Genetic Models for Long-Term Neurocognitive Outcomes in Pediatric Medulloblastoma and Traumatic Brain Injury

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Objective: Children who suffer from brain insults (i.e., traumatic brain injury (TBI), chemotherapy and radiation treatment for brain tumors) are susceptible to late-emerging cognitive sequelae. Even with similar neurological risk variables, variability in long-term cognitive outcomes remains an area of investigation for researchers of acquired brain injury. Given the potential for genetic factors to influence response to chemoradiation, researchers have examined associations between germline, inherited, single nucleotide polymorphisms (SNPs), and neurocognitive outcomes for cancer survivors. Children who sustain an uncomplicated mild TBI generally recover without long-term neuropsychological consequences. However, TBI survivors have overlapping mechanism categories with cancer survivors through secondary injury variables that can be influenced by genomic variation (e.g., oxidative stress and neuroinflammation). Furthermore, the study of genomic vulnerability is limited in heterogenous groups of pediatric TBI survivors. This study aims to identify associations between genotype and long-term neurocognitive outcomes for acquired brain injury survivors by utilizing machine learning to uncover pathophysiological similarities and differences between groups.
Participants and Methods: Fourteen brain tumor survivors, 139 traumatic brain injury survivors, and 63 healthy, age-matched controls completed the Letter N-back task to obtain performances on core neurocognitive skills (attention, working memory, and processing speed). Ten targeted genotypes were examined across five pathophysiological pathways (neurotransmission, oxidative stress, neuroinflammation, plasticity, growth and repair, and folate metabolism). Data were trained and tested utilizing three regression machine learning models. Mean estimated error and R^2 were generated for each neurocognitive

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outcome. A feature importance score for models with positive variance was generated to determine how predictive a given SNP is for neurocognitive outcomes.
Results: Genotype only accounted for a small amount of variance in cognitive outcomes when all clinical groups were combined. The mean absolute error for the best-fitting models from analyses where all groups were combined decreased when groups were examined separately; however, the differences in model R^2 values were not significant. The relationship between brain tumor survivors and processing speed performance depended on genotype. Two SNPs had positive feature importance at the interaction level (rs58225473 and rs1801394). These SNPs are located on the CACNB2 and MTR genes and have functional consequences for neurotransmission and folate metabolism. Models of traumatic brain injury survivors did not explain positive variance and could not be examined for feature importance. Additionally, even when removing the only mechanism of action that should not be relevant for TBI survivors (folate metabolism polymorphisms), the TBI models still did not explain positive variance.
Conclusions: Findings of the importance of two key SNPs on MTR and CACNB2 genes align with recent systematic reviews, which found associations between these polymorphisms and neuropsychological outcomes in more than one group or cohort of pediatric cancer survivors. Models for TBI survivors were limited by the heterogeneity of the group and ceiling effects on performance. An understanding of genetic vulnerabilities influenced by treatment and injury-related factors in acquired brain injury will inform our understanding of the developing and recovering childhood brain. The current study is an initial contribution to this goal and highlights the utility of machine learning methodology for future studies that examine the influence of genetic heterogeneity in pediatric acquired brain injury.

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57 Executive Functioning Correlates with Adaptive Behaviors in Wiedemann-Steiner Syndrome

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Objective: Wiedemann-Steiner syndrome (WSS) is a rare Mendelian disorder of epigenetic machinery caused by a mutation in KMT2A, with hallmark features that include intellectual disability and developmental delay. Animal models have helped identify the critical roles KMT2A plays in prefrontal neuron maturation and executive function (i.e. working memory) development. However, the neurobehavioral phenotype of individuals with WSS, including executive functioning, remains poorly characterized. Accordingly, this study aimed to 1.) examine the neurobehavioral profile (adaptive, psychosocial, and executive functioning) associated with WSS and 2.) the correlations between executive functioning and these domains.
Participants and Methods: A total of 25 mothers of individuals with WSS (13 females, Mean age=12.78 years, SD=7.88) completed a combination of parent-informant questionnaires. The caregivers completed the Adaptive Behavior Assessment System 3rd Edition (ABAS-3), the Strengths and Difficulties Questionnaire (SDQ), and a version of the Behavior Rating Inventory of Executive Function (BRIEF). Descriptive analyses were conducted to examine proportion of the sample with clinically significant concerns on the BRIEF and SDQ, and low to very low adaptive skills based on ratings on the ABAS-3. Partial correlations were computed to examine the relationships between overall executive functioning (BRIEF General Executive Composite, GEC) with adaptive domains (ABAS-3 Conceptual, Practical, Social), and psychosocial functioning (SDQ Emotional Problems, Conduct Problems, Hyperactivity, Peer Relations, Prosocial Behaviors) while accounting for age. Associations that survived Benjamin Hochberg correction are reported.
Results: Of our sample, 64% were rated in the very elevated range for executive functioning problems (BRIEF GEC), with a greater

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