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.

Categories: Genetics/Genetic Disorders
Keyword 1: brain tumor
Keyword 2: child brain injury
Keyword 3: pediatric neuropsychology
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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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proportion endorsing clinically significant concerns with behavior regulation (68%) relative to cognitive regulation (48%). Majority of participants was rated in the low or very low range for ABAS-3 General Adaptive Composite (72%), with a greater proportion showing problems in Practical (64%) and Conceptual Domains (64%) relative to Social Domain (44%). Among those who completed the SDQ, caregiver ratings implicate elevated Total Problems (90%) with greater concerns observed in Emotional Problems (62%), Hyperactivity (81%) and Peer Relationship difficulties (95%). After controlling for age, executive functioning difficulties were associated with weaker skills in the Conceptual (r=-0.56, p=0.003), Social (r=-0.44, p=0.028) and Practical domains (r=-0.51, p=0.009); as well as more Hyperactivity (r=0.49, p=0.025) and Conduct problems (r=0.58, p=0.007). Specifically, day-to-day challenges with executive functions were related to weaker adaptive skills in Self-Care (r=-0.54, p=0.006), Self-Direction (r=-0.53, p=0.007), and Communication (r=-0.49, p=0.01).
Conclusions: Individuals with WSS are at risk for executive functioning deficits, which in turn may impact the development of and/or day-to-day application of adaptive skills and behavior regulation. Future clinical research should further explore the development and neurophysiology of executive functions among those with WSS with multidisciplinary methods, including behavioral, cognitive and neurobiological metrics. Those working with individuals with WSS may consider executive functioning interventions, which may yield indirect benefits to self-regulation and daily use of life skills.

Categories: Genetics/Genetic Disorders
Keyword 1: adaptive functioning
Keyword 2: executive functions
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58 Parent Ratings of Internalizing and Externalizing Behaviors in Children with NF1 Across Childhood: A Longitudinal Investigation

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Objective: The purpose of the present study is to characterize the trajectory of internalizing and externalizing behaviors in children with NF1 longitudinally from the early childhood period to the school age period on a broad psychosocial norm-referenced measure using linear mixed model growth curves.
Participants and Methods: Children with NF1 (n=28) were seen at least once between the ages of 3-8 years old and then again between the ages of 9-13 years old. Parents completed the Behavior Assessment System for Children (BASC) Second Edition; the version of the BASC administered depended on age (i.e., preschool form or child form). Linear mixed model growth curve analyses were used to examine the developmental trajectories of children with NF1 on the following scales, which were selected due to findings in the literature: Externalizing Problems, Internalizing Problems, Hyperactivity, Anxiety, Depression, Attention, and Executive Function. T-scores (M=50, SD=10) were used. Higher scores indicate more challenges.
Results: By using loess lines to qualitatively describe the patterns of ratings across time, it is evident that most scales (Externalizing Problems, Internalizing Problems, Hyperactivity, Attention Problems, Executive Function) demonstrated curvilinear trajectory patterns, with scores peaking in the 8–10-year-old range, then decreasing again. However, there was no statistically significant effect of age on any of the scales. Notably, trajectories largely included standard scores within the normative range (T-scores between 45-55).
Conclusions: Overall, the models also suggest that most children with NF1 are within the average range of functioning on all scales examined across the childhood period. Furthermore, with the exception of the Depression and Anxiety scales, ratings tend to peak around the 8–10-year period, and then decrease into early adolescence. Thus, when working with patients with NF1, it may be the case that clinicians note relative increases in challenges across these domains in late childhood, though these challenges may decrease over time during this age range. Linear growth curve modeling identified that the developmental trajectories of internalizing and externalizing behaviors of children with NF1, as

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