Title: Stability and Predictive Value of Intellectual Functioning in Neurofibromatosis Type 1 beginning in the Preschool Years

Authors: G. Nathanael Schwarz,1 Christina L. Casnar,2 Brianna D. Yund,3 Kristin M. Lee,1 Natalie Brei,3 & Bonita P. Klein-Tasman1

1University of Wisconsin, Milwaukee, 2Children’s National Medical Center, 3Catholic Social Services

Introduction: Neurofibromatosis type 1 (NF1) is a rare genetic disorder that affects several aspects of cognitive functioning including intellectual functioning (IF) as well as attention and executive functioning. Cross-sectional studies and a small number of longitudinal studies suggest a moderate lowering of IF in youth with NF1 regardless of chronological age (Klein-Tasman et al., 2014; Nupan et al., 2017; Cutting et al., 2002). The stability and predictive value of IF in the preschool years to IF in the school-age and early adolescence years have not been examined in youth with NF1. Understanding of the predictive value of IF in the preschool years may be helpful in the assessment of early risk predictors and treatment planning. First, this study aims to describe the stability of IF in the preschool age. Secondly, it aims to examine the degree to which IF in the preschool years is predictive of IF between the ages of 9 and 13 in youth with NF1.

Method: Data were collected as part of a larger longitudinal study on the cognitive and behavioral phenotype in youth with NF1. The first time point was collected for children between ages 3 – 6. Twenty-three of these participants were also seen once for a follow up session between ages 9 and 13. Participants were included if they had two or more visits (N=47). As not every participant was seen at each age (3,4,5,6 and 9-13-yr-old follow up), N's varied between 15-23 depending on the analysis.

The Differential Ability Scales – Second Edition (DAS-II) was administered to participants at each assessment visit. The DAS-II is a comprehensive measure of cognitive abilities. The General Cognitive Ability (GCA) composite reflects overall cognitive functioning. Verbal and nonverbal reasoning factors are included for participants ages 2.5-3.4 years and verbal, nonverbal and spatial reasoning factors for all other children (ages 3.5+). Verbal Cluster (VC) and Nonverbal Reasoning Cluster (NVC) scores were also examined separately. All scores were standard scores with a mean of 100 and a standard deviation of 15.

Results: At visit 1 during the preschool years (3-5) DAS-II GCA had a mean of 92.49 (SD=12.09) and at the 9-13 year follow up a mean of 94.38 (SD=14.92). GCA scores in the preschool years (between ages 3-4.5-5-6) were moderately correlated from year to year (3-6, r’s.43-.65, p’s .047-.001). VC scores during the early to mid-preschool years were moderately correlated from year to year (ages 3-5, r’s .69-.82, p’s .<.001); but correlations from year to year during late preschool years were not significant (5 to 6, r=.32, p=.16). In contrast, NVC scores during preschool years were only significantly correlated from year to year in the late preschool age (5 to 6, r=.58, p=.007) and were not significantly correlated during the early and mid-preschool age (3-5, r’s.23-.35, p’s .18-.29). GCA scores at both ages 3-4 and 5-6 predicted GCA scores at age 9-13 (r’s .64-.68, p’s .0003-.01). Similarly, VC scores at ages 3-4 predicted VC scores at ages 9-13 (r=.53, p=.03) and 5-6 year old’s VC scores showed trend to predict VC at age 9-13 (r=.41, p=.052). In contrast, NVC scores from either 3-4 or 5-6 year time point did not significantly predict NVC scores at age 9-13 (r’s .24-.38, p’s .17-.29). Analysis using growth curve modeling is in process.

Discussion: This longitudinal study is the first to describe the stability and predictive value of IF in youth with NF1. Both general IF and verbal functioning showed moderate stability during the preschool years in children with NF1 similar to that observed in unaffected children (Scheider et al.,1999). However, measurement of nonverbal reasoning was not stable across the early preschool years and achieved significant stability only in late preschool years. General and verbal functioning in the preschool years (but not nonverbal reasoning) predicted respective functioning in the school age and early adolescence years. Both general IF and verbal functioning difficulties in the preschool years may be useful to predict which youth with NF1 are at risk for decrements in IF in the school age and early adolescence years.

References/Citations: