Title: Characterizing Problem Behaviors in Neurogenetic Syndromes during Toddlerhood

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Introduction: Comorbid problem behaviors and psychopathology are often associated with neurogenetic syndromes and affect family functioning and quality of life substantially (Hodapp & Dykens, 2007; Reilly, Murtagh, & Senior, 2015). Characterizing early behavioral phenotypes and psychopathology can therefore provide insights on syndrome-specific screening and treatment for these individuals and their families. Yet, there has been relatively little research on the emergence of problem behaviors in neurogenetic syndromes during infancy and toddlerhood. To address this need, the present study contrasted parent-reported problem behaviors in toddlers and young children with Angelman syndrome (AS), Prader-Willi syndrome (PWS), and Williams syndrome (WS) against low-risk controls without known neurogenetic syndromes (LR). By focusing on toddlers and young children, as well as examining multiple neurogenetic syndromes concurrently, this study was well suited to explore the differential early development of problem behaviors and their preclinical presentation profiles, informing stronger models for clinical care in early childhood.

Method: 109 toddlers and young children between 18 and 48 months of age participated in the study (LR: n = 35; AS: n = 21; PWS: n = 23; WS: n = 30). Age and sex were similar across groups (age: Kruskal-Wallis $\chi^2 (3) = 0.45, p = .929$; sex: $X^2 (3) = 1.78, p = .620)$. As part of an ongoing longitudinal study at Purdue University, participants’ parents completed the preschool version of the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2000), a widely used measure for assessing problems in behavioral, emotional, and social functioning. The CBCL yields scores for total problems, two broadband internalizing and externalizing scales, seven narrowband scales, and five DSM-oriented scales. We first used Wilcoxon-Mann-Whitney tests to examine atypicalities in problem behaviors, where total problems, broadband, narrowband, and DSM-oriented raw scores were expected to be higher in neurogenetic syndromes. We then used Fisher’s exact tests to examine whether the proportion of children with scores in publisher-derived borderline or clinical ranges was higher in neurogenetic syndromes.

Results: Total problems were elevated in AS and WS, (AS: $z = 3.12, p = .002$; WS: $z = 2.80, p = .005$), but not in PWS ($z = 0.25, p = .805$). At the broadband level, these patterns were somewhat specific to internalizing problems (AS: $z = 4.28, p < .001$; WS: $z = 2.96, p = .003$; PWS: $z = 0.02, p = .987$), with more similar externalizing problems across neurogenetic syndromes and LR controls ($ps > .166$). In terms of narrowband scales, all three neurogenetic syndromes were rated as displaying more withdrawn behavior (AS: $z = 6.14$; PWS: $z = 4.39$; WS: $z = 5.85, ps < .001$). Also, both AS and WS displayed more attention problems (AS: $z = 4.70, p < .001$; WS: $z = 3.14, p = .002$) and WS displayed more somatic complaints ($z = 2.98, p = .003$). In terms of DSM-oriented scales, all three neurogenetic syndromes displayed more autism spectrum problems (AS: $z = 6.03$; PWS: $z = 3.67$; WS: $z = 3.84, ps < .001$). Also, both AS and WS displayed more depressive (AS: $z = 3.27, p = .001$; WS: $z = 2.97, p = .003$) and attention deficit hyperactivity problems (AS: $z = 3.87$; WS: $z = 3.35, ps < .001$).

Elevated problem behaviors in neurogenetic syndromes generally did not exceed borderline/clinical thresholds, consistent with the young age of the sample. However, Fisher’s exact tests revealed that the proportion of children with borderline/clinical scores was significantly higher in AS than LR controls for internalizing, withdrawn, depressive, autism spectrum ($ps = .005$), and attention problems ($p < .001$). Final analyses will extend these preliminary results by exploring potential sub-group similarities and differences across genetic risk, as well as predictions of group membership based on cross-syndrome problem behavior profiles.

Discussion: Substantial atypicalities in problem behaviors emerged early in AS and WS, but not in PWS, highlighting distinct cross-syndrome risk profiles that may warrant distinct clinical approaches to child treatment and family support. Although similar domains of problem behaviors were implicated in AS and WS, there were marked differences in severity; several problem behaviors in AS were of clinical significance (e.g., 71% with borderline/clinical scores for attention problems), which coincided with clinical impressions of severe functional impairments in AS. The transition from preclinical to clinical profiles of problem behaviors warrants further study. Future research should employ longitudinal approaches to investigate the trajectories of
problem behaviors across early development, as well as the relationships between early childhood problem behaviors and long-
term behavioral and psychopathological outcomes. The characterization of problem behaviors in neurogenetic syndromes during
infancy and toddlerhood not only enhances our theoretical understanding of these neurodevelopmental disorders, but also
facilitates earlier identification and more timely and precise intervention to benefit these children and their families.

References/Citations:

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