

Title: Understanding Communication Outcomes of Children with Angelman Syndrome using the Observer-Reported Measure of Communication Ability (ORCA)

Authors: Lisa Hamrick¹, Amanda Seidl¹, & Bridgette Kelleher¹

Introduction: Children with Angelman syndrome (AS) are known to demonstrate significant delays in expressive language (Grieco et al., 2019), making it challenging to characterize early communication development in this population. These difficulties can have severe consequences for clinical trials, which require sensitive measures that can capture meaningful change in communication ability in response to treatments. The Observer-Reported Measure of Communication Ability (ORCA; Lucas et al., 2019, Zigler et al., 2020) was recently developed as an AS-specific measure of communication ability. The ORCA is a 73-item parent-report measure that captures communication abilities across expressive, receptive, and pragmatic communication domains. ORCA items were developed based on interviews with communication experts and caregivers of individuals with AS. Items are categorized into conceptual ability levels that were confirmed by a group of speech-language pathologists. The ORCA outputs both concept-level ability scores and a single *t*-score ($M=50$, $SD=10$) representing the individual's overall communication ability, scaled using IRT models based on a sample of 295 responses from caregivers of individuals with AS. However, it is not yet clear how scores on the ORCA relate to other indicators of vocal development in this population. Here, we leveraged an extant database from an ongoing, longitudinal study to test whether three distinct indicators of early communication predict later ORCA scores in children with AS.

Method: Participants were 17 children diagnosed with AS (11 male) enrolled in the Purdue Early Phenotype Study, an ongoing longitudinal study of early development of children with neurogenetic syndromes. Participation involves online surveys every 6-12 months as well as a phone interview and a daylong recording of the child's language environment. ORCAs were collected at the child's most recent online survey ($M=54.01$ months, $SD=11.15$, 31.51-73.92) and compared to three measures of social communication, collected earlier in development, that represented a range of constructs and assessment formats. (1) The Vineland Adaptive Behavior Scales, Third Edition (VL-3) was used to assess adaptive skills; we analyzed scaled scores (SS) and growth scale values (GSV) of the receptive and expressive language subscales of the VL-3, as well as the Adaptive Behavior Composite (ABC) and standard scores in the Communication and Socialization domains. (2) The Language Environment Analysis (LENA) system was used to collect the daylong recording of the child's language environment and produce measures of language complexity; we used the Child Vocalization Count (CVC), Automated Vocalization Analysis (AVA), and Vocal Productivity (VP) standard scores in analyses, as well as Canonical Babbling Ratio calculated from selected segments of the recording. (3) The Communicative Development Inventory (CDI) was used to assess lexical diversity and comprehension; we analyzed the Words Understood and Words Produced counts. Because we relied on extant data, ORCAs were collected approximately 21 months after the VL-3 ($SD=5.48$, 17-33), 20 months after the LENA ($SD=0.86$, 18-21), and 21 months after the CDI ($SD=4.57$, 12-30).

Results: Analyses were conducted in R version 4.0.2. We conducted partial Spearman's rank correlations of VL-3, LENA and CDI variables with ORCA *t*-scores, covarying the age difference between when the two measures were collected and correcting for multiple comparisons using the Holm-Bonferroni Correction. ORCA scores in our sample were lower than average ($M=42.61$, $SD=9.51$, 30.63-62.74). The ORCA demonstrated strong positive associations with the VL-3 Receptive Language subdomain (SS : $\rho=.79$, $p'=.007$; GSV : $\rho=.72$, $p'=.025$), Socialization domain ($\rho=.73$, $p'=.020$), and Adaptive Behavior Composite ($\rho=.74$, $p'=.020$). The association with the VL-3 Communication domain was non-significant after correcting for multiple comparisons ($\rho=.62$, $p'=.124$). The ORCA was not associated with VL-3 EL scores or with any LENA or CDI variables (all ρ 's $< .44$, all p 's $> .116$, all adjusted p 's $> .928$). However, it is notable that AVA, VL-3 EL, and Words Produced were positively skewed (skews > 1) and demonstrated significant floor effects.

Discussion: Overall, the ORCA demonstrated a unique pattern of associations with communication skills measured earlier in development. Two key findings emerged. First, ORCA outcome scores were more strongly associated with early receptive language skills (as measured by the VL-3) than expressive language skills (as measured by the VL-3, LENA, and CDI). These

findings suggest that aspects of early expressive language skills – including lexical diversity, vocal maturity, and adaptive use of expressive communication – may not be strong predictors of overall communication ability in AS. Importantly, although low expressive language is expected in children with AS, the restricted range and floor effects observed in our sample likely statistically contribute to the null findings in this study. Our second key finding is that ORCA outcomes were also associated with early social and adaptive skills more broadly, which may reflect that pragmatic communication skills are captured in each of these measures. Together, these findings help us better understand how variation in early communication skills may be later reflected in overall communication ability within the AS population; specifically, it appears that early receptive and pragmatic skills may be more relevant to communication outcomes in AS than expressive language skills.

References:

- Grieco, J. C., Romero, B., Flood, E., Cabo, R., & Visootsak, J. (2019). A conceptual model of Angelman syndrome and review of relevant clinical outcomes assessments (COAs). *The Patient-Patient-Centered Outcomes Research*, 12(1), 97-112.
- Lucas, N., McFatrach, M., Zigler, C.K., Berent, A., Evans, P., Gordon, K., Jones, H.N., Panagoulas, J. and Reeve, B.B., 2019, October. Designing measures of communication ability in individuals with Angelman syndrome [abstract]. In *QUALITY OF LIFE RESEARCH* (Vol. 28, pp. S117-S117).
- Zigler, C.K., Lin, L., Lucas, N., McFatrach, M., Berent, A., Evans, P., Gordon, K., Jones, H., Panagoulas, J., & Reeve, B.B., 2020, October. The Observer-Reported Communication Ability (ORCA) measure: Validation for use in clinical trials for individuals with Angelman syndrome [abstract]. International Society for Quality of Life Research 27th Annual Conference, Virtual.

Funding for the development of the ORCA was provided by Duke University and the Foundation for Angelman Syndrome Therapeutics (FAST). Funding for this study was provided by NIH (F31DC018219, K23MH111955) and the Kinley Trust.

¹ Purdue University, West Lafayette, Indiana