

Title: Social Communication Outcomes: Use of the Brief Outcome Measure of Social Communication (BOSCC) in Minimally Verbal Children with Fragile X syndrome

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Introduction: Fragile X syndrome, the most common cause of inherited intellectual disability, is caused by a mutation in a single gene on the X chromosome. Individuals with FXS often present with notable developmental challenges, with difficulties in expressive language development and social interaction skills among the most prominent. Because language and social communication play a critical role in learning, social functioning, and daily living skills, these are high priority endpoints for treatment studies in FXS. However, evaluation of treatment efficacy in FXS is hampered by a lack of validated clinical outcome assessments (COA). Indeed, although several drugs yielded substantial phenotypic improvements in mouse models of FXS, these findings have generally failed to translate into successful human clinical trials (Berry-Kravis et al., 2013). Berry-Kravis et al. (2013) attributed this failure in part to a lack of appropriate outcome measures and a failure to initiate treatments early in development. Thus, there is a need for validated COA to measure changes in social communication in the context of future therapeutic clinical trials of FXS. Building on over two decades of previous research with the Autism Diagnostic Observation Schedule, the BOSCC was created by Catherine Lord and colleagues (Cornell University) for use in autism spectrum disorder (ASD). Results from studies including individuals with ASD suggest that the BOSCC is a promising measure that is more sensitive to subtle social communication changes over time than other measures such as the ADOS-2 (Kitzerow et al., 2015; Grzadzinski et al., 2016; Pijl et al., 2016). Despite these promising results, this measure has not been utilized with other diagnoses with social communication impairments, such as FXS. In the present study, the primary objective was to examine the initial psychometric properties of the BOSCC in minimally verbal children with FXS, specifically establishing test-retest reliability, construct validity, and feasibility of multisite collection and establishment of a central reader for scoring.

Method: Participants were 18 full-mutation males with FXS, ranging in age from 3 – 8 years ($M = 4.50$ years, $SD = 1.54$), seen at one of two testing sites in the United States. In addition, based on caregiver report, all participants were minimally verbal (i.e., ranging from single word language to the initial use of phrase speech) and came from primarily English-speaking households. All participants were seen for both a test and a retest visit, which occurred on consecutive days. The BOSCC for minimally verbal individuals (BOSCC-MV) was administered at each study visit and scored by a blind centralized team of expert clinician coders looking at the videos. The BOSCC-MV total score, Social Communication (SC) domain, Restricted and Repetitive Behavior (RRB) domain, and Core domain (which encompasses both the SC and RRB domains) scores were considered. In addition, the ADOS-2, Social Responsivity Scale-2, Aberrant Behavior Checklist – Community, and the Vineland-3 were administered to assess construct validity.

Results: The estimated inter-rater reliability (ICC) determined for the 2 expert raters at Visit 1 was 0.887 (95% CI: 0.706, 0.960) for the total BOSCC-MV score, 0.873 (95% CI: 0.673, 0.955) for the BOSCC-MV SC domain, and 0.868 (95% CI: 0.652, 0.954) for the BOSCC-MV Core domain. For the RRB domain, inter-rater reliability was slightly less at 0.713 (95% CI: 0.350, 0.892). The estimated test-retest reliability (ICC) measured across 2 consecutive visits (Visit 1 and Visit 2) was 0.765 (95% CI: 0.458, 0.906) for the total BOSCC-MV score. Test-retest reliability was similar for the SC domain (0.779, 95% CI: 0.488, 0.912) and for the Core domain (0.757, 95% CI: 0.438, 0.904), but was lower for the RRB domain (0.491, 95% CI: 0.065, 0.771). With regard to convergent validity, the BOSCC-MV total and domain scores were found to be moderately correlated with the ADOS-2 Total and Domains scores ($r_s = 0.582$ to 0.657) and with the Vineland-3 Communication scores ($r_s = -.503$ to $-.569$). Weak to no associations were observed between the BOSCC-MV scores and the scores generated by the SRS-2 or the ABC-C.

Discussion: The overall results show the feasibility of implementing the BOSCC for minimally verbal individuals in a multisite study when administered by trained personnel and scored by experienced central readers. The levels of test-retest and inter-rater reliability demonstrated in the present sample of youth with FXS are comparable to those reported in previous studies with ASD populations. The BOSCC scores showed good convergent validity with other SC measures (e.g., ADOS-2 SC domain, Vineland-

3 communication domains); however, correlations with other measures were smaller. This suggests that the information between these measures are not entirely overlapping and thus can be used complementarily in future studies. These data suggest that the BOSCC is a promising measure to assess social communication in minimally verbal youth with FXS. Future studies should consider evaluating the utility of the BOSCC in a larger sample that potentially includes a wider range of language/module levels to evaluate the psychometric properties of the BOSCC more thoroughly in FXS.

References:

- Berry-Kravis, E., Hessel, D., Abbeduto, L., Reiss, A. L., Beckel-Mitchener, A., Urv, T. K., & Groups, O. M. W. (2013). Outcome measures for clinical trials in fragile X syndrome. *Journal of developmental and behavioral pediatrics*, 34(7), 508.
- Kitzerow, J., Teufel, K., Wilker, C., & Freitag, C. M. (2016). Using the brief observation of social communication change (BOSCC) to measure autism-specific development. *Autism Research*, 9(9), 940-950.
- Grzadzinski, R., Carr, T., Colombi, C., McGuire, K., Dufek, S., Pickles, A., & Lord, C. (2016). Measuring changes in social communication behaviors: preliminary development of the Brief Observation of Social Communication Change (BOSCC). *Journal of autism and developmental disorders*, 46(7), 2464-2479.
- Pijl, M. K., Rommelse, N. N., Hendriks, M., De Korte, M. W., Buitelaar, J. K., & Oosterling, I. J. (2018). Does the Brief Observation of Social Communication Change help moving forward in measuring change in early autism intervention studies? *Autism*, 22(2), 216-226.

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