

Assessing Autism Diagnostic Tools in Fragile X Syndrome



Eileen Haebig, Audra Sterling & Susen Schroeder

Waisman Center and Department of Communication Sciences & Disorders, The University of Wisconsin-Madison

Background

- Fragile X syndrome (FXS) is the leading cause of inherited intellectual disability, affecting approximately 1 in every 2,500 males (Hagerman, 2002).
- A significant number of males with FXS also meet the criteria for autism (25-30%) and a substantial majority display autistic-like behaviors (e.g., repetitive behaviors, language perseverations, etc.; Hatton et al., 2006).
- Assessments for diagnosing autism spectrum disorder (e.g., ADOS, ADI-R, CARS2) were designed for idiopathic autism, and have not been systematically evaluated in other clinical populations, such as FXS.

Research Questions:

- Do two different examiner observation tools (ADOS and CARS2) and a parent interview (ADI-R) demonstrate high agreement in assessing diagnostic criteria for autism in children with FXS?
- How do observational measures of autism symptoms relate to cognitive and language abilities in children with FXS?

Methods

- Participants
 - School-age males with FXS (N = 15)
- Autism Assessment
 - Examiner Observation
 - Autism Diagnostic Observation Schedule (ADOS)
 - Child Autism Rating Scale 2nd Edition (CARS2)
 - Parent Interview
 - Autism Diagnostic Interview – Revised (ADI-R)
- Nonverbal Cognition
 - Leiter – R Brief IQ
- Receptive Vocabulary
 - Peabody Picture Vocabulary Test 4th Edition (PPVT-4)
- Expressive Vocabulary
 - Expressive Vocabulary Test 2nd Edition (EVT-2)

Results

Scores from each autism diagnostic tool were derived and each child was assigned to the corresponding diagnostic category. See Table 1 for a comparison of diagnostic classification per diagnostic tool and for participant characteristics. Figure 1 depicts the proportion of autism diagnoses children with FXS received according to the CARS2, ADOS, and ADI-R.

Table 1: Participant Characteristics

| Participant | CARS2 Dx | ADOS Dx | ADI-R Dx | Nonverbal Cognition | Receptive Vocabulary | Expressive Vocabulary | Chronological Age |
|-------------|-----------|-----------------|-----------|---------------------|----------------------|-----------------------|-------------------|
| FXS 01 | Autism | Autism | Autism | 36 | 33 | 36 | 10.25 |
| FXS 02 | No Autism | Autism | Autism | 56 | 65 | 57 | 9.25 |
| FXS 03 | Autism | Autism Spectrum | No Autism | 48 | 60 | 51 | 16.42 |
| FXS 04 | Autism | Autism | Autism | 36 | 44 | 42 | 15.01 |
| FXS 05 | No Autism | Autism | Autism | 44 | 74 | 73 | 14.7 |
| FXS 06 | Autism | Autism | No Autism | 56 | 82 | 83 | 15.03 |
| FXS 07 | No Autism | Autism Spectrum | No Autism | 54 | 75 | 77 | 9.04 |
| FXS 08 | Autism | Autism | MD | 52 | 54 | 66 | 9.06 |
| FXS 09 | No Autism | Autism Spectrum | Autism | 60 | 67 | 75 | 12.0 |
| FXS 10 | No Autism | Autism | Autism | 42 | 60 | 62 | 12.42 |
| FXS 11 | No Autism | Autism | Autism | 52 | 67 | 74 | 13.58 |
| FXS 12 | Autism | Autism | Autism | 40 | 71 | 72 | 12.33 |
| FXS 13 | Autism | Autism | No Autism | 38 | 54 | 44 | 13.75 |
| FXS 14 | Autism | Autism | Autism | 48 | 35 | 59 | 10.08 |
| FXS 15 | No Autism | Autism Spectrum | Autism | 50 | 79 | 72 | 12.25 |

Figure 1. Proportion of Diagnostic Categorization by Assessment Tool

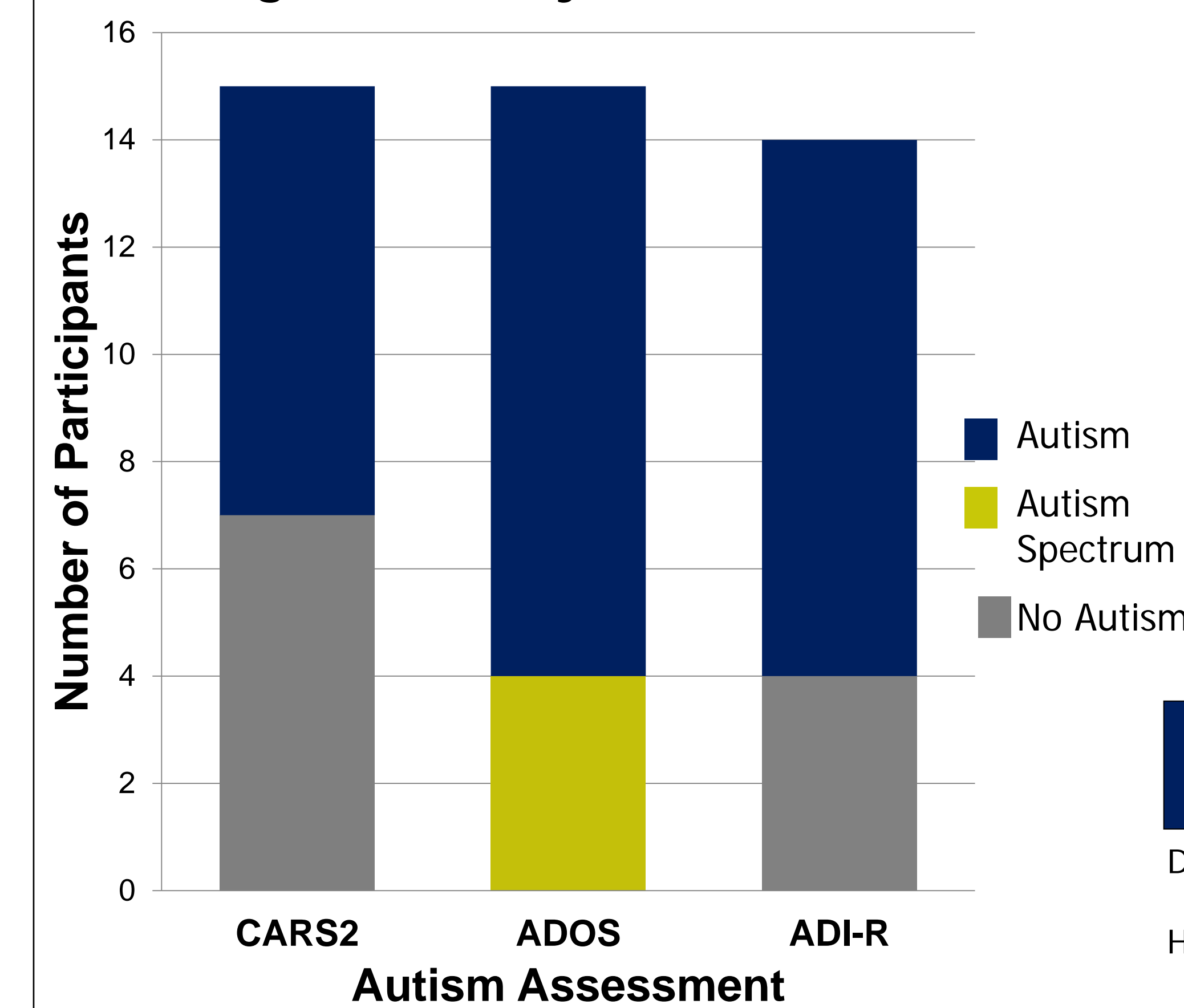


Table 2 demonstrates that the CARS2 and the ADOS are highly correlated. Additionally, the relationship between autism scores and other abilities (e.g., nonverbal cognition and vocabulary) are shown.

Table 2. Bivariate Correlations

| Variable | 1 | 2 | 3 | 4 | 5 |
|--------------------------|---|-------|-------|-------|-------|
| 1. CARS-2 Total Score | | .85** | -.60* | -.52* | -.36 |
| 2. ADOS Total Score | | | -.54* | -.47 | -.47 |
| 3. Receptive Vocabulary | | | | .82** | .54* |
| 4. Expressive Vocabulary | | | | | .69** |
| 5. Nonverbal Cognition | | | | | |

Discussion

- Correlations between the CARS2 and the ADOS scores suggest that both assessments measure similar characteristics in children with FXS. Despite this, the CARS2 and the ADOS agreed in only 8 of the 15 children with FXS (53%).
- The ADI-R agreed with the ADOS diagnosis on 71% of the sample, whereas it only agreed with the CARS2 diagnosis on 36% of the cases.
- The CARS2 does not differentiate between autism and autism spectrum disorder.
- It is possible that the ADOS over diagnoses autism in FXS given that all of the children met diagnostic criteria.
- Nonverbal cognitive abilities do not appear to be a factor that drives autism diagnoses; however, language abilities may.
- Our limited sample sizes needs to be expanded to provide more conclusive results.
- The ADI-R could be compared to the CARS2-QPC parent measure in this population.

References

Dunn, L. M., & Dunn, D. M. (2007). *Peabody Picture Vocabulary Test, Fourth Edition*. Bloomington, MN: Pearson.

Hagerman, R. J. (2002). The physical and behavioral phenotype. In R. J. Hagerman & P. J. Hagerman (Eds.), *Fragile X syndrome: Diagnosis, treatment, and research* (pp.3-109). Baltimore: Johns Hopkins University Press.

Hatton, D. D., Sideris, J., Skinner, M., Mankowski, J., Bailey, D.B., Roberts, J., & Mirrett, P. (2006). Autistic behavior in children with fragile X syndrome: Prevalence, stability, and the impact of FMRP. *American Journal of Medical Genetics Part A, 140A* (17), 1804-1813.

Lord, C., Rutter, M., DiLavore, P., & Risi, S. (2001). *Autism diagnostic observation schedule*. Los Angeles: Western Psychological Services.

Lord, C., Rutter, M., & Le Couteur, A. (1994). Autism Diagnostic Interview-Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism Developmental Disorders, 24*, 659-685.

Roid, G. H., & Miller, L. J. (1997). *Leiter International Performance Scale-Revised*. Wood Dale, IL: Stoelting.

Schopler, E., Van Bourgondien, M.E., Wellman, G.J., & Love, S.R., (2010). *Childhood autism rating scale, Second Edition*. Bloomington, MN: Pearson.

Williams, K. T. (2007). *Expressive vocabulary test* (2nd ed.). Minneapolis, MN: Pearson.

Acknowledgments

We are extremely appreciative of the families who participated in this study and the lab members who worked on this project, without whom our research would not have been possible.

Funding for this project was provided by NIH including R03 DC011616 and start-up funds from the University of Wisconsin-Madison. We are grateful for the support from the Waisman Center Core Grant (P30 HD03352, M. Mailick, PI).