Social Communication and Interaction Deficits in Boys with a Fragile X Premutation

Ariel Zucker[1,2], Sarah L Nolin[3], Anne Glicksman[3], Nicole Tortora[3], Mohammad Arif[3], Stephanie Sherman[4], Emily Graves Allen[4], Jessica E Hunter[5], Amanda Kenepp[1,2], Shira Russell-Giller[1,2], Veronica J Hinton[1,2]

[1]Queens College, City University of New York, Flushing, NY, USA.
[2]The Graduate Center, City University of New York, New York, NY, USA.
[3]NYS Institute for Basic Research in Developmental Disabilities, Staten Island, NY, USA.
[4]Emory University School of Medicine, Atlanta, GA, USA.
[5]RTI International, Research Triangle Park, NC, USA

Objective

Approximately 14% of males and 5% of females with Fragile X Syndrome (defined as >200 CGG repeats on the X-linked FMR1 gene) are diagnosed with Autism Spectrum Disorder (ASD). Less is known about phenotype of children with a fragile X premutation (CGG expansions between 55 and 200 repeats). Many studies have found an increased prevalence of ASD in children with the PM compared to controls, but interpretation is limited by ascertainment bias (i.e., those who present with symptoms are evaluated) and small sample size. The current study is designed to examine social communication behaviors in a large sample of non-referred children with the premutation.

Hypotheses

1. Children with a PM will be more likely to have a parent-reported diagnosis of ASD than controls.
2. Both boys and girls with the PM will demonstrate more parent-reported difficulties on Social Responsiveness Scale, Second Edition (SRS-2) compared to controls.
3. Parent-reported difficulties on the SRS-2 will be associated with CGG length.

Methods

- 254 participants included children ages 3-11 who were identified prenatally as carrying PM or normal allele.
- Parents reported 'yes' or 'no' to existing ASD diagnosis (PM carrier males n = 2, non-carrier males n = 1, PM carrier females n = 0, non-carrier females n = 0).
- Parents-reported social communication was measured with the Social Responsiveness Scale, Second Edition (SRS-2 preschool and school-age editions).

Participants (N=254)

	PM Carrier	Non-carrier
Male	74	66
Female	49	65

The SRS-2

- 5 subscales:
  - Social Motivation
  - Social Awareness
  - Social Cognition
  - Social Communication
  - Restricted Interests and Repetitive Behavior
- 2 DSM-5 compatible composite scores
  - Social Communication and Interaction
  - Restricted Interests and Repetitive Behavior
- Total Score

Analyses

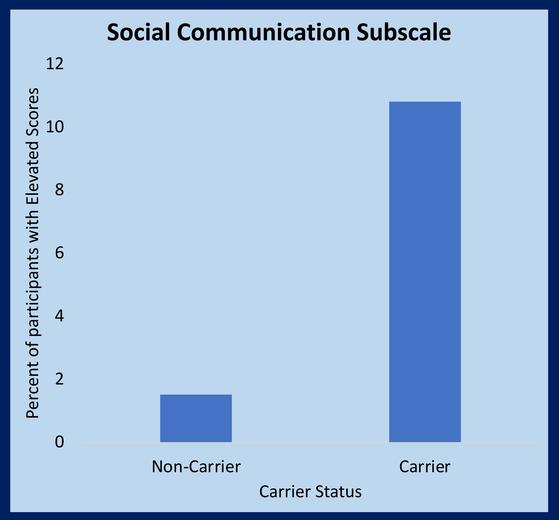
- T-scores from each scale were transformed into dichotomous variables based on cutoffs ($t < 60$; $t \geq 60$).
- Fisher's exact tests were conducted to compare percent of sample falling above cutoff on SRS-2 scales in PM carriers versus controls.
- Exploratory correlational analyses examined association of CGG repeat size with significant findings.

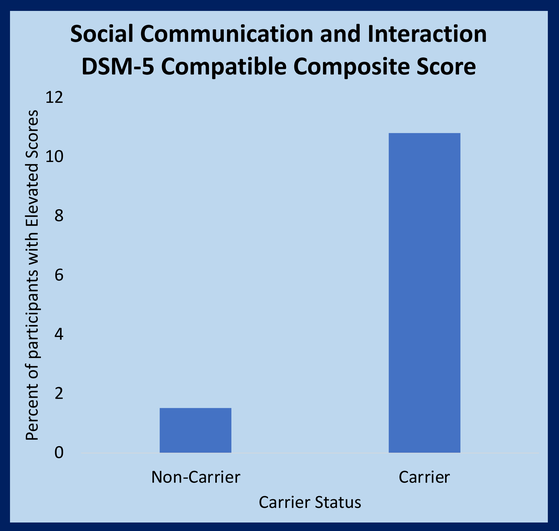
Results

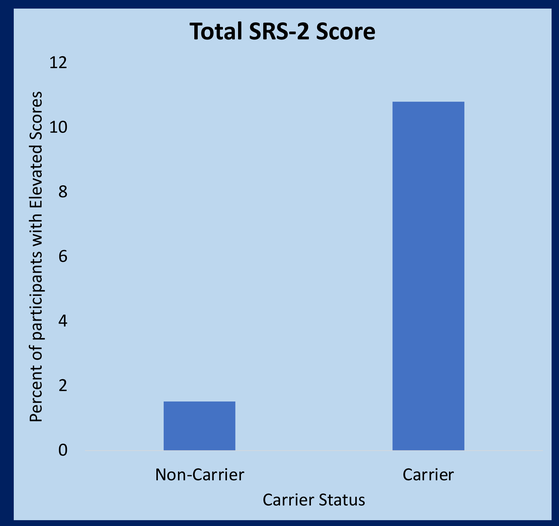
- Results demonstrated there was **no between-group difference on parent-report of ASD**.
- On the SRS-2, **male PM carriers showed significantly elevated scores compared to non-carriers on the Social Communication subscale** (1.52% compared to 10.81%; $p = .036$, Fisher's exact test; odds ratio = 7.88, 95% CI [0.96, 64.78]), **Social Communication and Interaction DSM-5 compatible composite score** (1.52% compared to 12.16%; $p = .019$, Fisher's exact test; odds ratio = 9.00, 95% CI [1.11, 73.09]), and the **Total score** (1.52% compared to 12.16%; $p = .019$, Fisher's exact test; odds ratio = 9.00, 95% CI [1.11, 73.09]).
- **No significant differences were identified on any of the SRS-2 scales for females.**
- Further, **CGG repeat size was not associated with SRS-2 findings**.

Conclusions

- Findings indicate that in a non-referred PM sample, **there is no increased report of ASD diagnosis**.
- On the standardized questionnaire, parents endorsed elevated social communication problems in male PM carriers compared to controls, although the **magnitude of social communication challenges observed are more subtle than those reported in prior studies**.
- Given that our sample is the largest, non-referred sample of PM children to date, the data confirm that **social communication problems do exist in PM boys, but in lower rates than previously reported**.







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