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Predictors of Quality of Life in Youth with Fragile X Syndrome

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Background

What is Fragile X Syndrome (FXS)?

- FXS is an X-linked dominant developmental disorder that affects approximately 1/4000 males and 1/4000 to 1/8000 females [2,6].
- Symptoms most commonly associated with FXS include:
  - Anxiety
  - Attention deficit/hyperactivity disorder (ADHD)
  - Obsessive-compulsive disorder (OCD)
  - Intellectual Disability (ID)
  - Self-injurious behavior
  - Aggression towards others [1]
- FXS is caused by a CGG repeat in the 5' untranslated region of the FMR1 gene on the X chromosome [3].

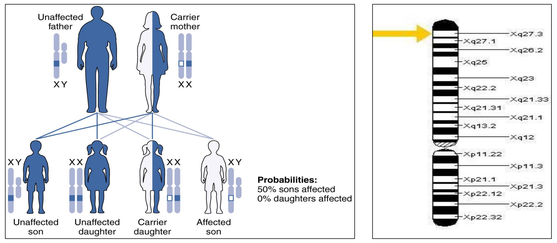

Figure 1. (Left) Diagram of genetic inheritance for FXS . (Right) X chromosome with yellow arrow indicating site of FMR1 mutation at Xq27.3.

Why is Quality of Life Important?

- Use of health-related quality of life (HR-QOL) measures in clinical practice has grown significantly in the last ten years [10].
- Numerous studies have been conducted surrounding HR-QOL in populations with ID, but none have focused explicitly on individuals with FXS. This is of particular importance when the challenging behavioral symptoms that accompany FXS are taken into consideration [4].

Why Use Pediatric Quality of Life Inventory (PedsQL)?

- PedsQL is used for assessing HR-QOL in healthy children and children with chronic health concerns [5].
- PedsQL proved to be reliable and valid in clinical trials of populations with acute and chronic diseases, implying that it is a useful device in the measurement and subsequent improvement in HR-QOL in these populations [9].

Why Find Phenotypic Correlates?

- Due to the high degree of variance in clinical presentation, accurately assessing HR-QOL in the FXS population is difficult.
- Clinicians want to accurately tell families which behaviors in FXS significantly correlate with enhanced or diminished HR-QOL, and then aggressively treat those issues that negatively impact HR-QOL.

Purpose and Aims

Purpose and Immediate Aim:

To identify phenotypic predictors/correlates of QOL in youth with FXS.

Long-Term Aim:

To gather a large body of data on phenotypic correlates of QOL in FXS and use this to quantify treatment progress in areas of impairments and behaviors known to negatively affect QOL in this population.

Figure 2. Research plan with immediate and long-term aims.

Methods

Data Acquisition

Data was extracted from the IRB-approved Developmental Disabilities Clinical Repository (DDCR) RedCap database at CCHMC. This repository holds phenotypic data and peripheral biological samples for individuals diagnosed with a developmental disability (DD), their first degree relatives, and non-DD control subjects.

- **Sample:** 27 individuals (18 males, 9 females) with FXS were pulled from the DDCR for analysis. Ages ranged from 2.92-21.08 years (M=11, SD= 5.5).
- **Measures**: Parents of each individual completed several phenotypic measures during participation in DDCR research:
  - PedsQL Parent Report for Children survey
  - PedsQL Parent Report Family Impact Module survey
  - Social Responsiveness Scale (SRS)
  - Aberrant Behavior Checklist (ABC)
  - Vineland Adaptive Behavior Scale (VABS)

Data Analysis

Descriptive statistics were generated from the collected body of data. Repeated measures ANOVA testing and partial correlation analyses were run where designated.

- **Variables:**
  - Totals for each of the PedsQL Parent Report for Children score domains (Physical, Emotional, Social, and School)
  - PedsQL Parent Report for Children total score (Mean Child QOL)
  - PedsQL Parent Report Family Impact Module total score (Family QOL)
  - VABS Adaptive Behavior Composite score (Vineland Adaptive)
  - Total SRS score
  - Totals for each of the 5 ABC score domains (Irritability, Lethargy, Stereotype, Hyperactivity, and Inappropriate Speech)

Results

Figure 3. Mean Differences Between the Four Domains of HR-QOL in PedsQL Parent Report for Children Across Age and Sex. "**" and "*" designate significant differences ($p < .05$) between means found in follow-up analyses as a result of significant main and interaction effects from within-subjects ANOVA. "**" superscript is significantly larger than "*" superscript. Larger values indicate higher QOL.

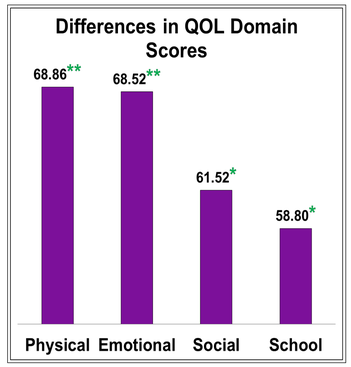

Table 1. Partial Correlations between Each of the Four Dimensions of HR-QOL and Other Dimensions of Quality of Life and Phenotyping Measures Controlling for Age and Sex. Numbers in purple text indicate strong significant correlations, while numbers in green text indicate mild significant correlations.

	Dimensions of Health Quality of Life			
	Physical	Emotional	Social	School
Mean Child QOL	**.83*** **	**.70*** **	**.61** **	**.67*** **
Family QOL	.03	**.44***	**.38***	**.50***
Vineland Adaptive	**.60** **	.08	-.05	.08
Total SRS	**-.32***	-.32	**-.59** **	**-.46** **
ABC Irritability	-.13	**-.44***	-.27	**-.45***
ABC Lethargy	-.29	-.20	**-.49** **	**-.49** **
ABC Stereotype	-.25	-.15	**-.39***	**-.42***
ABC Hyperactivity	.07	**-.38***	-.19	**-.33***
ABC Inappropriate Speech	**.38***	-.11	**-.43***	-.08
*** p < .05; ** p <.01; *** p < .001**				

Table 2. Partial Correlations between Mean Child and Family Dimensions of HR-QOL and Outcome Measures Controlling for Age and Sex. Numbers in purple text indicate strong significant correlations, while numbers in green text indicate mild significant correlations.

	Quality of Life	
	Mean Child	Family
Vineland Adaptive	**.41***	.14
Total SRS	**-.53** **	-.35
ABC Irritability	-.36	**-.66*** **
ABC Lethargy	**-.46***	.06
ABC Stereotype	**-.40***	-.25
ABC Hyperactivity	-.20	**-.43***
ABC Speech	.05	-.04
***p < .05. ** p <.01; *** p < .001**		

Discussion

Major Findings

- Social and School QOL are areas of reduced QOL in youth with FXS compared to Physical and Emotional Domains.
- Mean Child QOL and each domain of HR-QOL are strongly correlated in youth with FXS.
- High levels of irritability marked by aggression and self-injury negatively correlate with Family QOL in families of youth with FXS.
- Significant social impairment negatively correlates with QOL in youth with FXS.
- **Scores from phenotypic measures may be used to identify HR-QOL-associated areas for targeted clinical treatment.**

Limitations

- Due to a small sample size (N=27), statistical results cannot readily extrapolate to general population of FXS. However, correlations found in analysis trend nicely with clinical observations.

Further Experimentation

- Future studies should (1) include a larger sample size and (2) be supplemented with phenotypic data such as IQ.
- Test-retest data is needed with the PedsQL in FXS before it can be effectively used as a treatment outcome.
- Longitudinal PedsQL data is needed over time to characterize any potential developmental trajectories of QOL in persons with FXS and their families.

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Acknowledgements

This research is supported by Cincinnati Children's Hospital Medical Center (CCHMC) and was conducted within the Behavioral and Developmental Neuropsychiatry (BDNP) group within the Division of Psychiatry, CCHMC.