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Effects of Sertraline Treatment for Young Children with FXS

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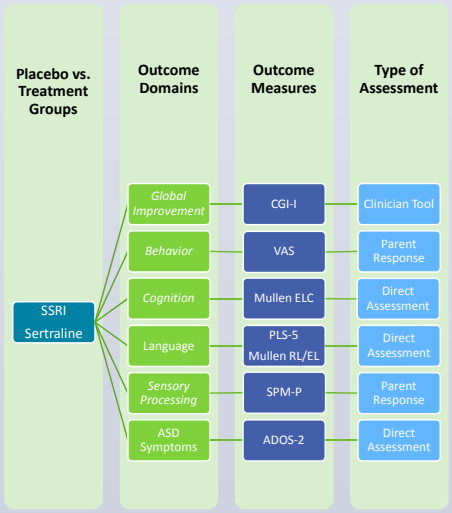
INTRODUCTION and PURPOSE

Selective serotonin reuptake inhibitors (SSRIs) help treat many of the phenotypic manifestations of fragile X syndrome (FXS) including anxiety, sensory processing challenges, and communication and intellectual deficits. However, the efficacy of SSRIs has not been previously studied in children with FXS under five-years-old. The purpose of this study was to elucidate group differences in behavior and developmental outcome measures for young children with FXS when treated with sertraline compared to placebo.

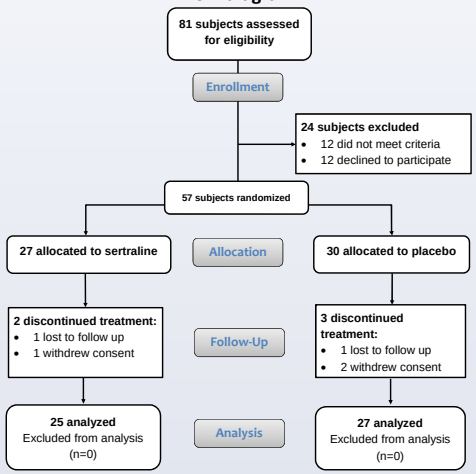
PARTICIPANTS and DESIGN

- 57 participants with FXS, ages 2 -6 years old (mean 3.9 years; SD 1.1)
- Randomized, 6-month, double-blind, placebo-controlled trial of sertraline (Zoloft)
- Baseline and post-treatment outcomes measured
- Primary outcomes: Mullen Scales of Early Learning (MSEL) expressive language subscales and Clinical Global Impression Scale-Improvement (CGI-I)
- Secondary outcomes: MSEL fine motor, visual reception, and receptive language subscales; Autism Diagnostic Observation Schedule, Second Ed. (ADOS-2); Visual Analog Scale (VAS); Sensory Processing Measure-Preschool (SPM-P); and Preschool Language Scale, Fifth Ed. (PLS-5)



RESULTS

Consolidated Standards of Reporting Trials (CONSORT) flow diagram

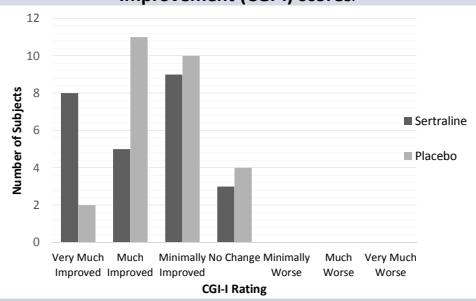


Primary Outcome Results

Variables	Sertraline						Placebo						
	Baseline			Follow Up			Baseline			Follow Up			
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	P-value[a]
MSEL													
Exp Lang Raw Score	26	21.3	10.3	25	25.0	10.8	30	19.3	9.7	27	21.3	9.6	0.586
Exp Lang T-Score	27	25.8	11.7	25	25.8	10.9	30	23.3	5.8	27	22.6	6.5	0.607
CGI-I	27	--	--	25	2.3	1.1	30	--	--	27	2.6	0.8	0.244

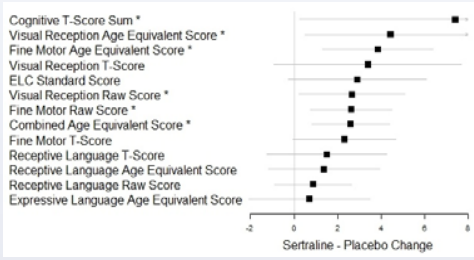
a- Adjusted significance level 0.016. MSEL – Mullen Scales of Early Learning; CGI-I – Clinical Global Impression Scale-Improvement

Distribution of Clinical Global Impression-Improvement (CGI-I) scores.



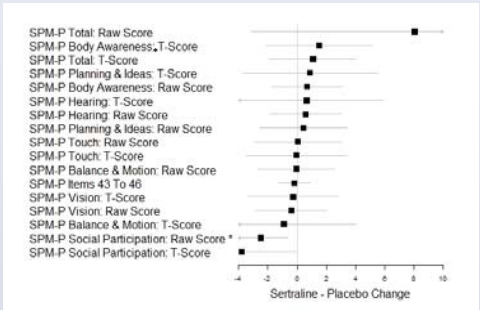
RESULTS

Effect Sizes of Sertraline on Mullen Scales of Early Learning Secondary Measures



Effect size are post treatment score difference estimates (sertraline minus placebo) adjusted for baseline measure, along with 95% CIs (arrows indicate CI length truncated for display). Asterisks indicate $P < 0.05$.

Effect Sizes of Sertraline on Sensory Processing Measure – Preschool (SPM-P)



Effect size are post treatment score difference estimates (sertraline minus placebo) adjusted for baseline measure, along with 95% CIs (arrows indicate CI length truncated for display). Asterisks indicate $P < 0.05$.

Comparison of Adverse Events

	Sertraline		Placebo		
Variable	No. of Patients	%	No. of Patients	%	P-value
Severity					
No Moderate/Severe AE	12	46.15	15	51.72	0.7891
Any Moderate/Severe AE	14	53.85	14	48.28	
Drug Related					
No drug related AE	5	19.23	6	20.69	1
Any drug related AE	21	80.77	23	79.31	
Serious Adverse Event					
No	26	100	29	100	--
Adverse Event Status					
No Ongoing	21	26	80.77	89.66	0.4548
Any Ongoing	5	3	19.23	10.34	

CONCLUSIONS

- This is the first known controlled trial of sertraline in young children with FXS.
- No significant differences were observed in the MSEL expressive language subscales and CGI-I primary outcome measures for sertraline when compared to placebo.
- Secondary measures revealed significant improvement in social participation on the SPM-P. Areas of fine motor and visual perception were also significantly improved on the MSEL when compared to age equivalent subjects. *Post hoc* analysis combining all MSEL age-equivalent scores (expressive, visual, receptive and fine motor) showed overall significant improvement.
- Results suggest sertraline had significant positive effect on social improvements and overall development.
- Adverse events (AEs) were similar between sertraline and placebo groups. No significant differences in characteristics of AEs were observed between both groups.

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