

# Fluoxetine and Sertraline Inhibit Height Growth During Puberty

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OBJECTIVE: To Characterize changes in height and weight in fluoxetine- vs. sertraline-treated youth undergoing pubertal growth

## INTRODUCTION

- Selective serotonin reuptake inhibitors (SSRI) are the first-line psychotropics for pediatric depressive and anxiety disorders [1-2].
- However, SSRIs have been associated with reduced growth in height, particularly in children undergoing puberty [3-6].
- This study examined SSRIs' effect on height growth and on Growth Hormone signaling in children in Tanner stages 2 through 4.

## MATERIALS & METHODS

- Following written informed consent, 66 medically healthy children, in Tanner stage 2 through 4, were enrolled prior to or within one month of starting fluoxetine or sertraline treatment.
- They underwent 3 visits (baseline and at Month 2 and 6), when their height and weight were measured and a fasting blood sample was collected to measure insulin growth factor-1 (IGF-1) and insulin growth factor binding protein 3 (IGFBP-3).
- Anthropometric data from 36 unmedicated healthy controls enrolled in an unrelated study were used for comparison.
- Age-sex-specific Z-score for height, weight, and body mass index (BMI) were generated.
- Patients with medical conditions or on medications that might interfere with height growth were excluded.
- Linear mixed effect modeling and generalized estimating equation (GEE) analyses evaluated the effect of SSRI use on age-sex-specific anthropometric measurements z-scores and on IGF1 and IGFBP-3 concentration, respectively.

## RESULTS & FINDINGS

Table 1: Demographic and Clinical Characteristics of the Participants

	Fluoxetine (n=39)	Sertraline (n=27)	SSRI Sample (n=66)	Controls (n=36)	p-value	p-value
Age, years	12.5 ± 1.6	13.1 ± 1.3	12.7 ± 1.5	12.6 ± 1.3	NS	NS
Female, n (%)	29 (74)	19 (70)	48 (73)	24 (67)	NS	NS
Tanner Stage (%; II/III/IV)	26/26/49	7/26/67	18/26/56	19/44/36	NS	NS
Height Z-Score	0.01 ± 0.94	0.20 ± 1.11	0.09 ± 1.01	0.39 ± 0.81	NS	NS
Weight Z-Score	0.16 ± 0.80	0.25 ± 0.82	0.20 ± 0.80	0.29 ± 0.73	NS	NS
BMI Z-Score	0.27 ± 0.61	0.24 ± 0.80	0.26 ± 0.69	0.16 ± 0.79	NS	NS
IGF-1, ng/mL	364.1 ± 204.3	348.1 ± 318.8	356.1 ± 254.0	---	NS	---
IGFBP-3, ng/mL (10 <sup>3</sup> )	4.1 ± 1.8	3.4 ± 1.7	3.8 ± 1.8	---	NS	---

Table 2: Parameter Estimates (±SEs) from the Linear Mixed Effects Regression Analysis Examining the Effect of Fluoxetine and Sertraline on the Anthropomorphic Measurements.

	Height Z-score	Weight Z-score	BMI Z-score
Baseline Z-Score	1.015 ± 0.012	0.990 ± 0.021	0.976 ± 0.028
Time	0.038 ± 0.070	-0.110 ± 0.108	-0.171 ± 0.126
SSRI Dose	0.064 ± 0.033	0.007 ± 0.049	-0.017 ± 0.057
SSRI Dose x Time x Group Interaction Effect	p=0.0633	p=0.1132	p=0.0305
Fluoxetine	-0.131 ± 0.103	0.148 ± 0.160	0.212 ± 0.185
Sertraline	-0.192 ± 0.083	0.255 ± 0.129	0.374 ± 0.149

Fluoxetine and Sertraline parameter estimates are in comparison to a slope of zero.  
Additional covariates included in model: sex, Tanner stage, and SSRI group.  
Bolded/green results are statistically significant (p<0.05) and italicized results are marginally significant (p<0.10).

Table 2 shows that sertraline dose was inversely associated with change in height Z-score over 6 months. This accounts for the positive association with BMI.

Table 3: Estimated Differences in Anthropomorphic Measurements (Raw Values) Between SSRI-Treated and Unmedicated Participants, at 6 Months, Using Different SSRI Doses.

SSRI Dose	ΔHeight (cm)	ΔWeight (kg)	ΔBMI (kg/m <sup>2</sup> )
0	+2.86 ± 0.17	+2.74 ± 0.37	+0.39 ± 0.13
0.5	+2.53 ± 0.16	+3.13 ± 0.35	+0.63 ± 0.12
2	+1.55 ± 0.55 <sup>a</sup>	+4.29 ± 1.19 <sup>b</sup>	+1.35 ± 0.42 <sup>c</sup>

All models included sex, Tanner stage, baseline anthropometric value, time, SSRI dose, and time x SSRI dose interaction effect.  
SSRI dose: Adherence-adjusted dose, with 1 unit = 20 mg of fluoxetine or 50mg of sertraline.  
<sup>a</sup>p<0.04 for difference between SSRI dose of 0 and 2 units at 6 months.  
<sup>b</sup>p>0.10 for difference between SSRI dose of 0 and 2 units at 6 months.  
<sup>c</sup>p<0.05 for difference between SSRI dose of 0 and 2 units at 6 months.

- Table 3 shows that a therapeutic dose of sertraline or fluoxetine for six months significantly reduces height growth and increases BMI gain.
- Using unmedicated healthy controls, the model estimates that SSRIs result in a failure to grow by about 1.5 cm over 6 months.
- Moreover, the SSRI dose was significantly inversely associated with IGF1 concentration ( $\beta$  = -63.5,  $p$  < 0.02) but not IGFBP-3 concentration ( $\beta$  = -200.3,  $p$  > 0.20).

## DISCUSSION & CONCLUSION

- Our data suggest that two commonly prescribed SSRIs hamper height growth and that this effect may be due to a reduction in IGF-1.
- Longer and larger studies are needed to determine the tempo of height growth failure during SSRI treatment, whether it is mediated by reduction in IGF-1, and whether adult height is impacted.

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