The Expression of IGF Type 1 Receptor is Increased in Obese Children

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Background

- Obese children are often taller than non-obese children before puberty.
- Reports on the GH/IGF system in obese children are not consistent and do not explain the increased height.
- Changes in IGF-I bioavailability/bioactivity have been claimed as a possible explanation, considering the high insulin levels observed in some children and the consequent lower IGFBP-1 concentrations.
- However, no data is available regarding the expression of the IGF type 1 receptor (IGF1R) in obese children.

AIM

To study the expression of IGF1R gene in obese children

Subjects and Methods

Subjects

- 29 obese children (BMI >2 SDS) with height > + 1 SDS (15 males)
- 18 non-obese (−2<BMI<+2 SDS) age-matched controls with height between −2 and +2 SDS (nine males).

All were prepubertal. None had any metabolic, endocrine, or genetic disease.

Table 1: Age, BMI and height (mean ± SDS) of obese and non-obese children

	Age (years)	BMI (SDS)	Height (SDS)
Obese	7.0 ± 1.4	3.2 ± 1.2	1.6 ± 0.6
Non-obese	7.3 ± 1.4	0.1 ± 0.8	-0.3 ± 0.6

Design

- Fasting blood samples were collected to analyse IGF1R gene expression in peripheral lymphocytes and determine the serum concentrations of IGF-I, IGFBP-3, ALS (acid-labile subunit) and insulin.

Assays

- Lymphocytes were isolated from other blood cells using Fycoll–Hypaque and the RNA extracted. The IGF1R mRNA expression was analyzed by quantitative real-time PCR.
- IGFI-I, IGFBP-3 (Immulite 2000, Siemens), ALS (DIAsource ImmunoAssays) and insulin were determined by specific immunoassays.

Statistical Analysis

- IGF-I was adjusted by age and sex (IGF-I ratio) dividing patients values by the median value for age and sex (Bedogni et al, 2012)
- Data were compared by t-test, Mann-Whitney and Fisher tests using the GraphPad Prism 6.0 (GraphPad Software Inc., San Diego, CA). P ≤ 0.05 was assumed as statistically significant.

Results

- The IGF1R mRNA expression ($2^{-\Delta\Delta CT}$) was higher in obese children than in non-obese controls (1.9 vs 1.15; *P*=0.02).
- IGF-I levels were also higher in obese children (237 vs. 143 ng/ml; *P*=0.001). No difference was found regarding IGFBP-3 levels.

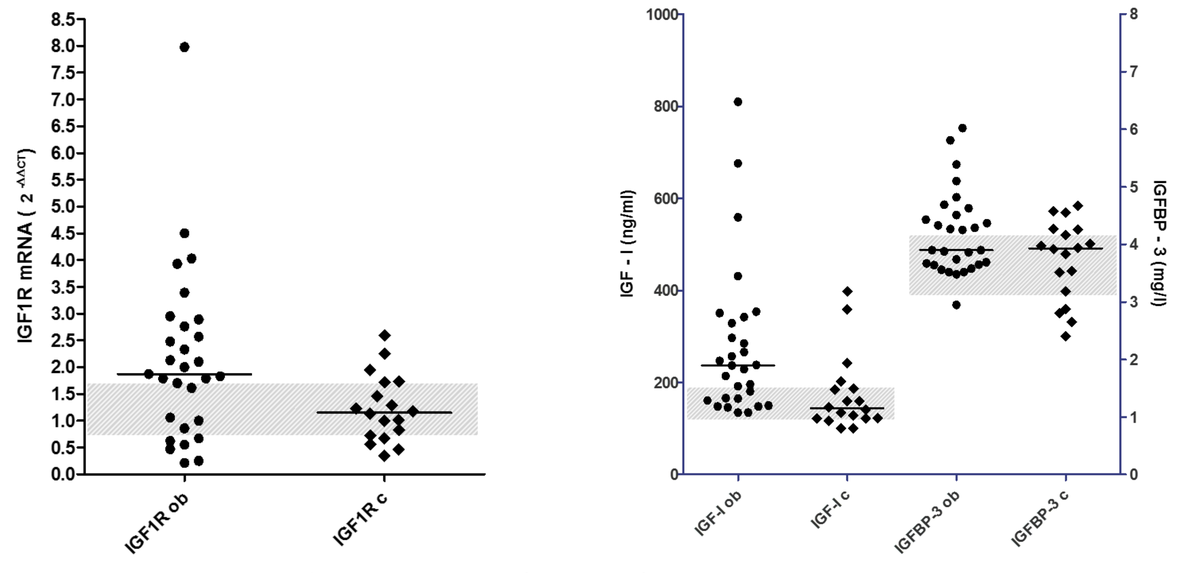

Figure 1: Expression of IGF1R mRNA (Panel A), serum IGF-I and IGFBP-3 concentrations (Panel B) in obese (ob) and non-obese (c) children. Bars represent medians. Shaded area represents interval between 25th and 75th percentiles of non-obese children's values.

- ALS levels were higher in obese children (175 vs. 155 mg/l; *P*=0.001).
- Insulin and HOMA-IR were also higher in obese children (*P*<0.0001)

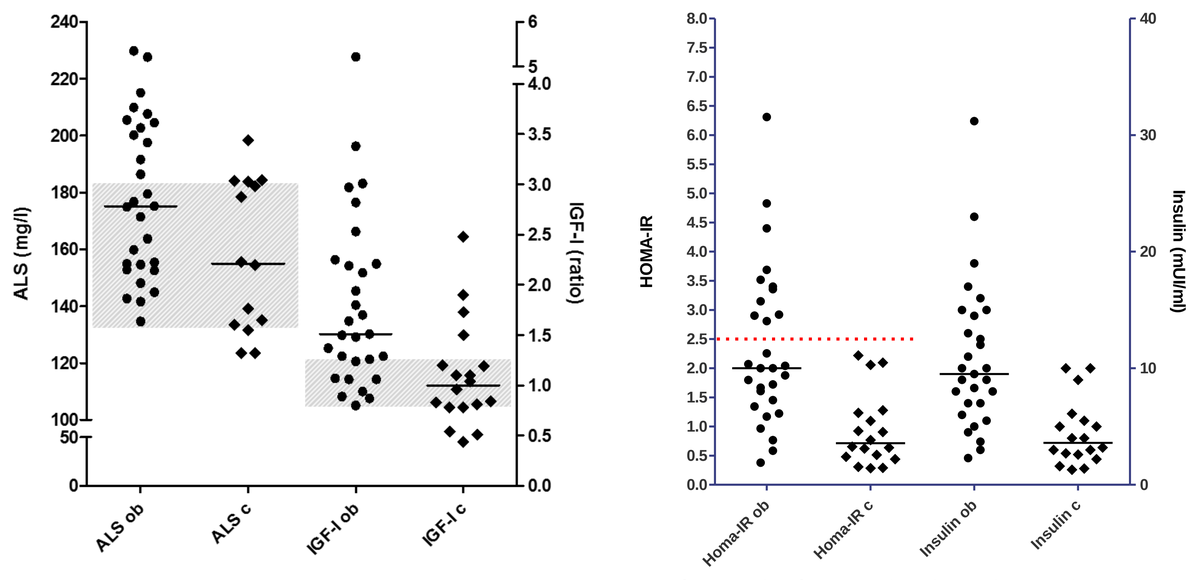

Figure 2: Serum ALS concentrations, IGF-I ratio (Panel A), insulin levels and HOMA-IR (Panel B) in obese (ob) and non-obese (c) children. Bars represent medians. Shaded area represents interval between 25th and 75th percentiles of non-obese children's values. Red doted line represents the suggested HOMA-IR cut-off for children.

Conclusion

- Obese children showed higher IGF1R mRNA expression and higher serum IGF-I levels than non-obese children.
- The higher expression of IGF1R and IGF-I levels may contribute to the increased height observed in many obese children.
- Differently from obese adults, in which GH secretion is decreased, the role of GH in the growth promotion of obese children is still unclear. Although ALS levels were also higher in these children, IGFBP-3 levels were not.
- However, we must consider that these last findings can reflect the higher sensitivity of IGF-I to GH changes.