

Body mass index negatively correlates with growth hormone response to GH provocation testing.

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Background

In adults it has been shown, that GHpeak values after provocation testing are negatively correlated to BMI¹. Preliminary studies in children have found a similar correlation^{2,3,4,5,6}. Consequently children with elevated BMI would be overdiagnosed with GH deficiency (GHD). However, studies so far were too small to define this correlation exactly. This would be a condition to judge whether and to what extent adjustments of GH cut-off levels should be considered also in children with elevated BMIs.

Objective

To study the correlation between BMI-SDS and the maximal GH serum levels reached in GH provocation tests in a larger cohort of children.

Patients and methods

We investigated children whose anthropometric data, pubertal status and laboratory findings had been documented in the Crescnet database. Of overall 1109 GH stimulation tests we retrospectively could analyze **524 children** and adolescents aged between 1 and 18 years with short-stature (height SDS<-2), who between 2004 and 2014 underwent a total of **735 GH provocation tests** (540 with arginine as a primary, and 195 with glucagon as a confirmatory test). Children with known syndromes (i.e. UTS), severe chronic illness or under antipsychotic or sex steroid medication were excluded from study. We applied a linear regression model to assess the correlation between **BMI-SDS** and the maximal GH serum value (**GHpeak**) reached during each test in the overall study group and then according to gender. To account for possible effects of puberty on GH secretion and BMI-SDS correlation we also studied the data according to **pubertal status** (prepubertal Boys: TV≤3ml, Girls: Tanner B>1). In prepubertal children we analyzed the data for correlations of GHpeak to BMI-SDS in the group of children without **GHD** (idiopathic-, SGA-, familial short stature and constitutional delay) and with **GHD** (including neurosecretory dysfunction). Cut-off level for GHD was 7,09 ng/ml. GH measurements were made with non-radioactive, chemiluminescent immunoassays⁷.

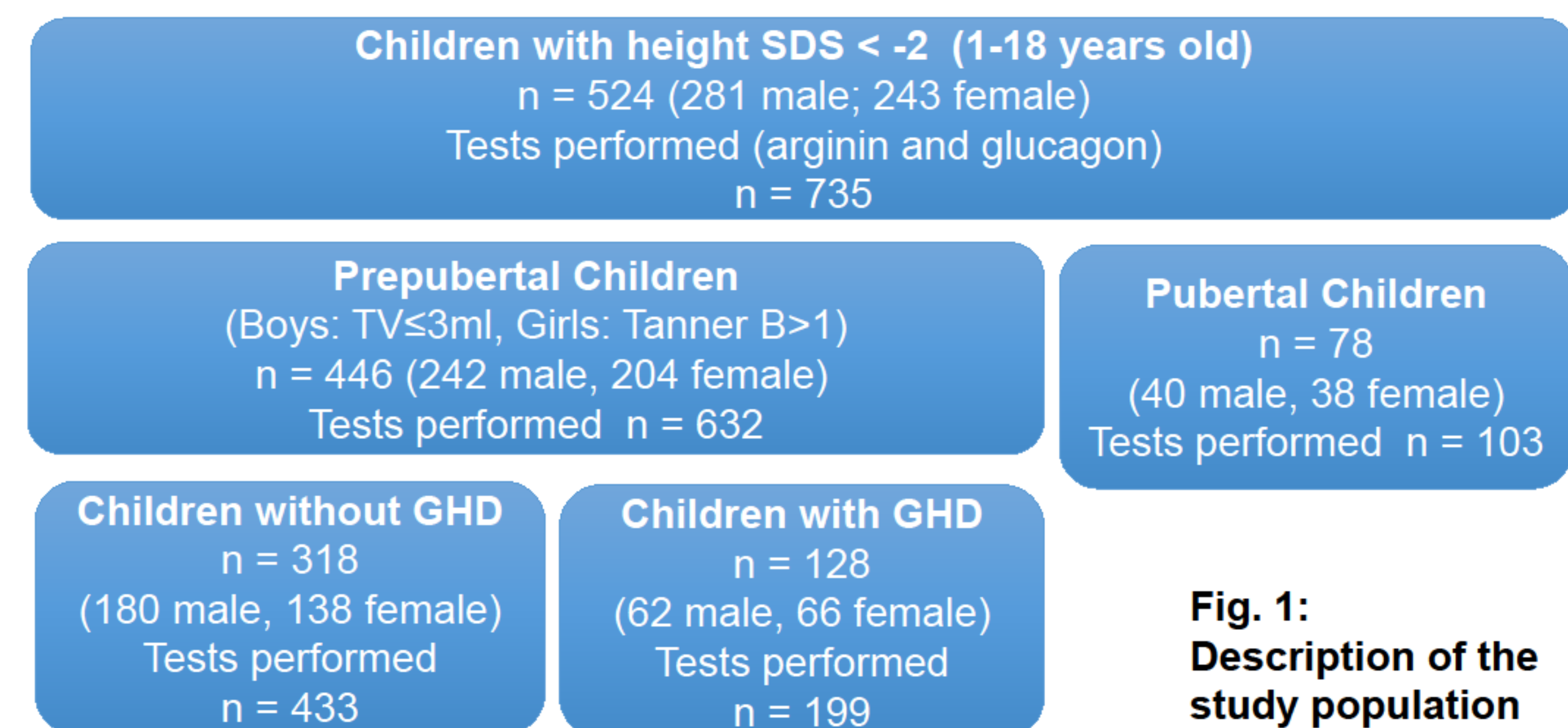


Fig. 1: Description of the study population

Results

There was a significant (negative) correlation of the BMI-SDS of the patient and the GHpeak (p<0,001) reached in the test (Fig 2a). This correlation was not different when studied according to gender (Fig 2b). The GHpeak in tests were not statistically different between test substances (Fig 3).

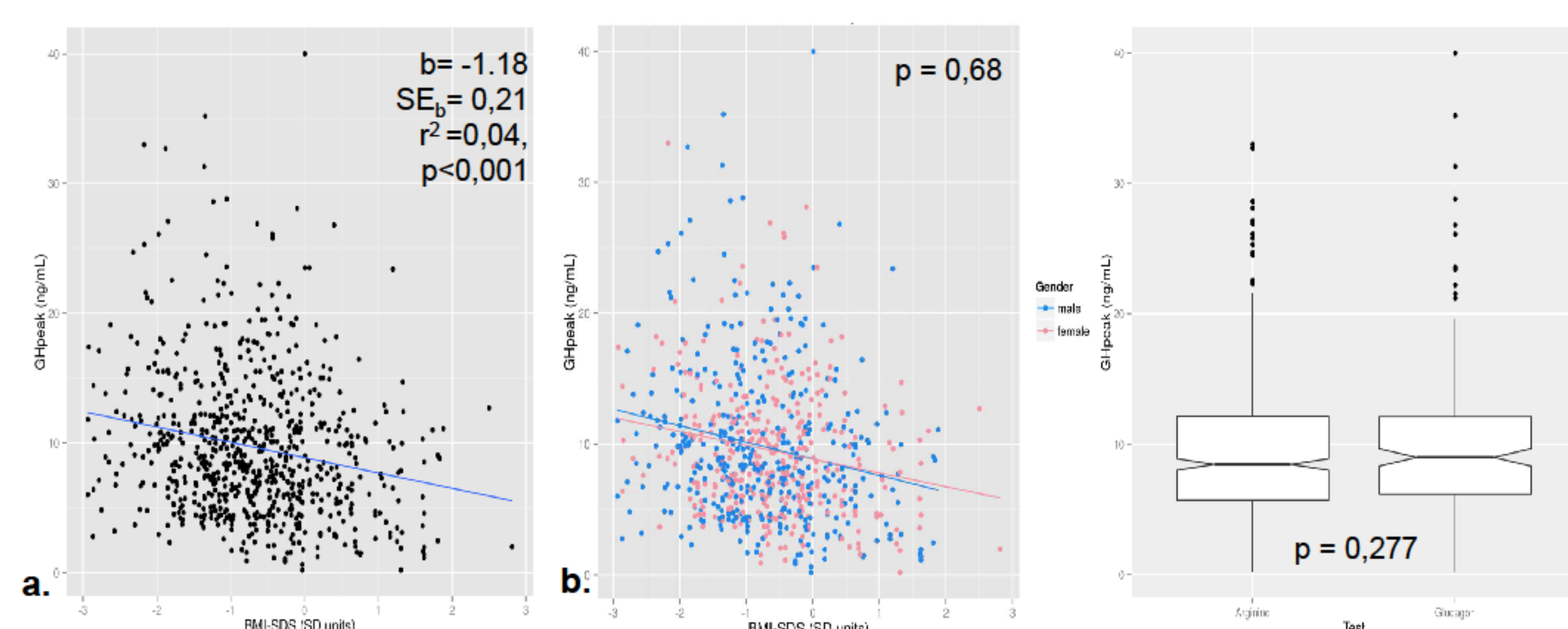


Fig 2: GHpeak vs. BMI-SDS
 a. in whole cohort, b. according to gender

Fig 3: GHpeak according to test substance in whole cohort

The effect of BMI on GHpeak is different in respect to pubertal status, although GHpeak or BMI-SDS levels are not significantly different between the 2 groups. (Fig. 4).

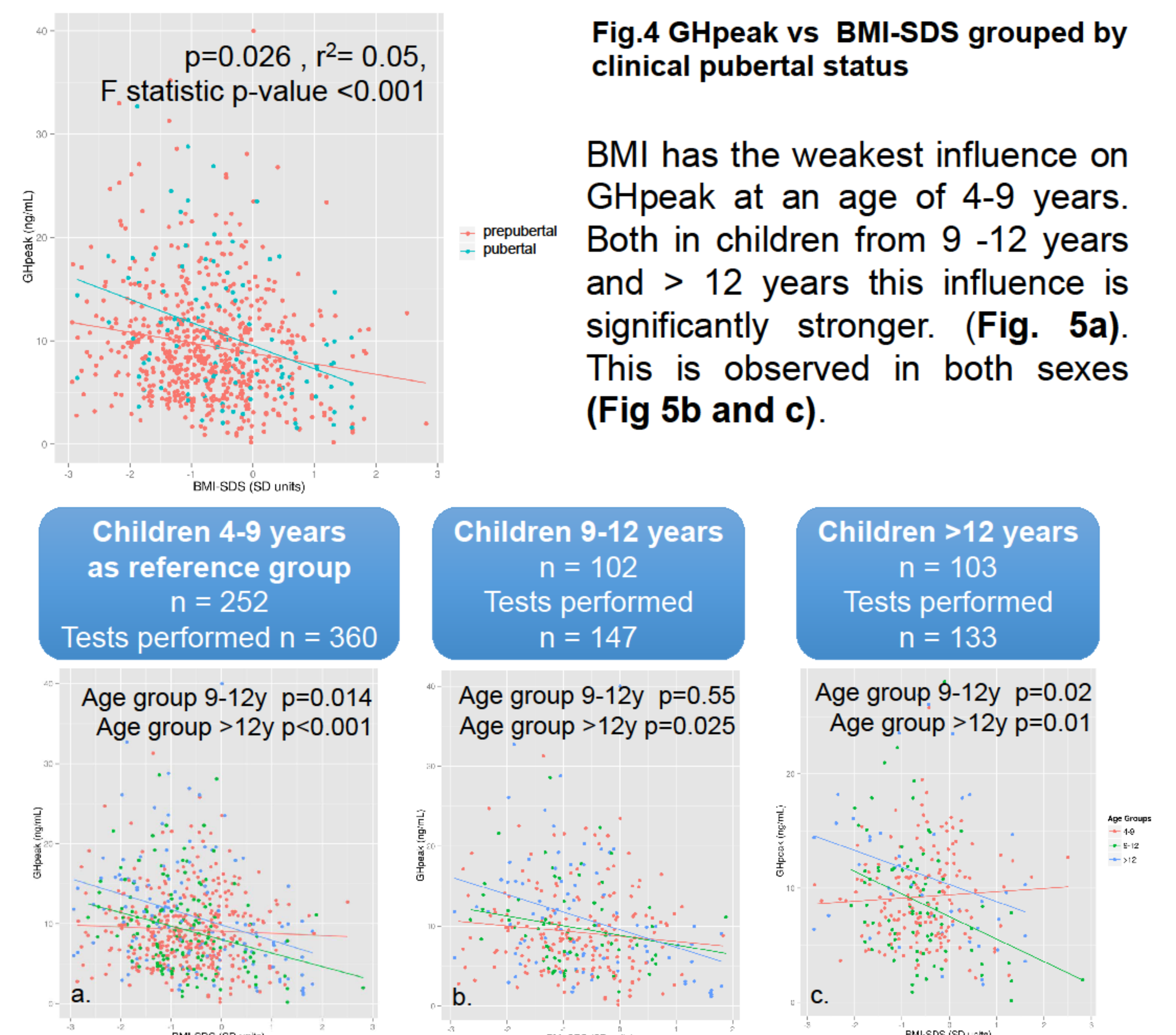


Fig.4 GHpeak vs BMI-SDS grouped by clinical pubertal status

BMI has the weakest influence on GHpeak at an age of 4-9 years. Both in children from 9 -12 years and > 12 years this influence is significantly stronger. (Fig. 5a). This is observed in both sexes (Fig 5b and c).

Fig 5: GHpeak vs. BMI-SDS between age groups a. whole cohort, b. males, c. females, r²: 0.08 , F statistic p<0,001

Finally, in prepubertal children no significant difference of this correlations (p=0,47 ,r²: 0,14, F statistic p < 0.001) was observed between children with and without GHD (Fig. 6).

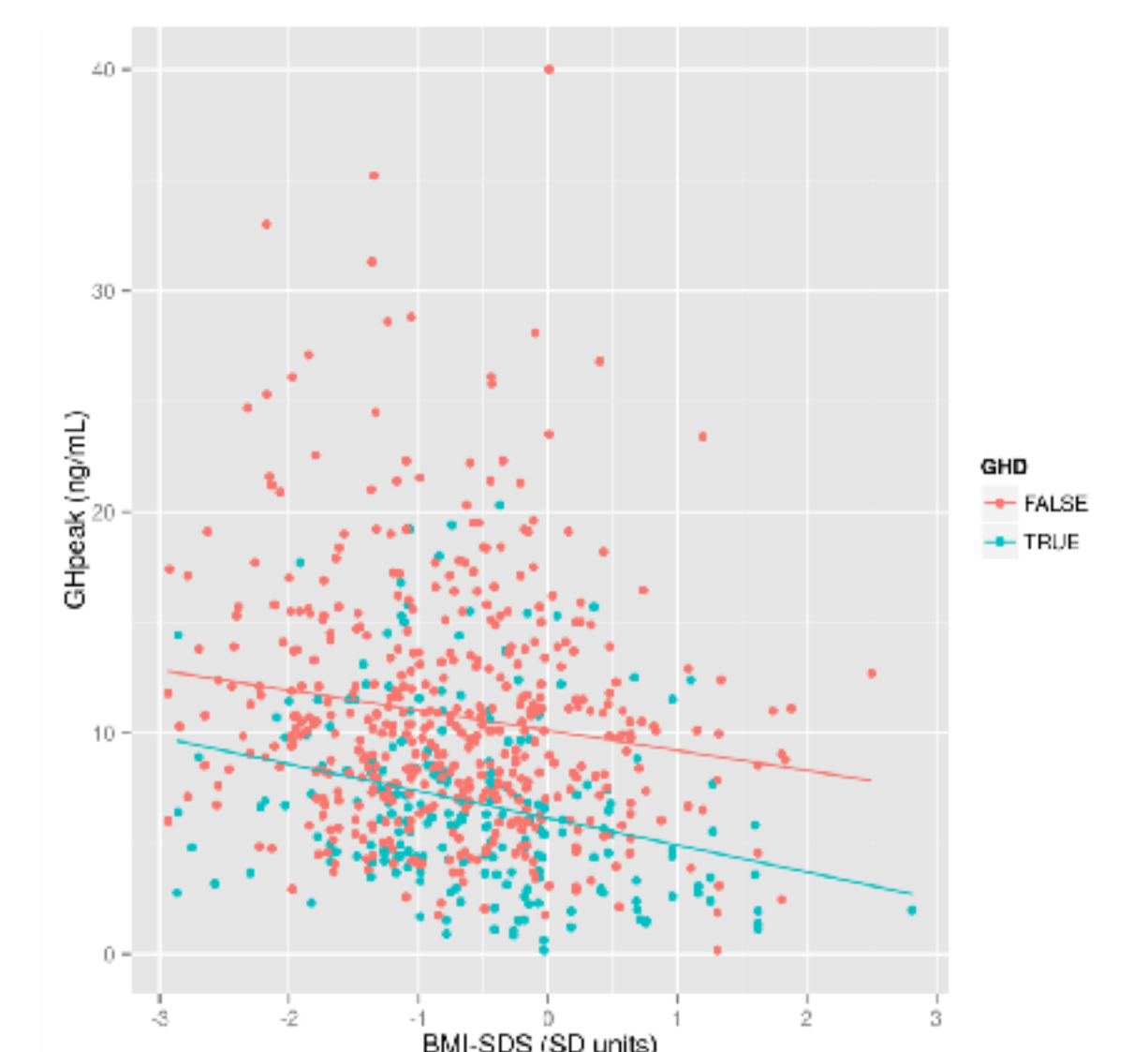


Fig 6: GHpeak vs. BMI-SDS in prepubertal non GHD and GHD children

Conclusion

- We found that the BMI significantly and negatively correlates with GHpeak values in both arginine and glucagon GH stimulation tests.
- As the effect BMI on GHpeak is age dependent and only weakly present in children aged 4-9 years, an adaption of cutoff levels for GHD according to BMI seems not appropriate in this age group.
- On the other hand, the influence of BMI on GHpeak increases significantly even before clinical signs of puberty are observed.
- The age from which BMI should be considered for making the diagnosis remains to be discussed.

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