Diagnosing GH deficiency in children by arginine HCl infusion test: relationship between auxological characteristics, arginine plasma profile and arginine-stimulated GH release

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BACKGROUND and OBJECTIVES

The diagnosis of isolated growth hormone (GH) deficiency is challenging, in particular due to the lack of a gold standard and the poor reproducibility of GH stimulation tests (1).

Arginine (Arg) HCl infusion is commonly used in the diagnostic workup of paediatric GH deficiency. Arginine infusion has been demonstrated to alter somatostatin tonus, whereas clonidine seems to exert its GH-releasing effect through increasing GHRH-stimulated GH release (2,3).

In adults a BMI-adjusted cut-off level in the diagnostic workup of GHD has been suggested for the Arg-GHRH test (4). In children however, the influence of body mass index (BMI) on systemic Arg concentrations and Arg-stimulated GH secretion following a weight-based Arg infusion protocol has not been systematically investigated.

We speculated that auxological parameters not only are associated with differences regarding susceptibility to GH-releasing stimuli, but that by using weight-based test protocols differences in body composition might also influence circulating Arg concentrations. Thus the aim of this study was to analyse whether auxological parameters modulate the Arg plasma concentration profile and associated GH secretion in short-statured prepubertal children undergoing Arg stimulation testing.

METHODS

Retrospective analysis, including 35 prepubertal short-statured children (24 male; age 10.1 ± 3.5 years; height SDS -3.1± 0.6, weight SDS -2.5± 1.0; BMI SDS -0.81± 0.2, preceding HV < P25). In prepubertal girls ≥ 8 years and prepubertal boys ≥ 10 years, GH stimulation testing was performed after sex steroid priming.

Arginine plasma concentration profile, following intravenous infusion of 0.5 g/kg Arg, was measured at time points -15, 0, 30, 45, 60, 90, 120 and 150 minutes, using a lithium high-resolution column (Biochrom 30 amino acid analyser).

hGH concentration was measured at the same time-points as described for Arg concentration by a highly sensitive ELISA (Mediagnost, Germany).
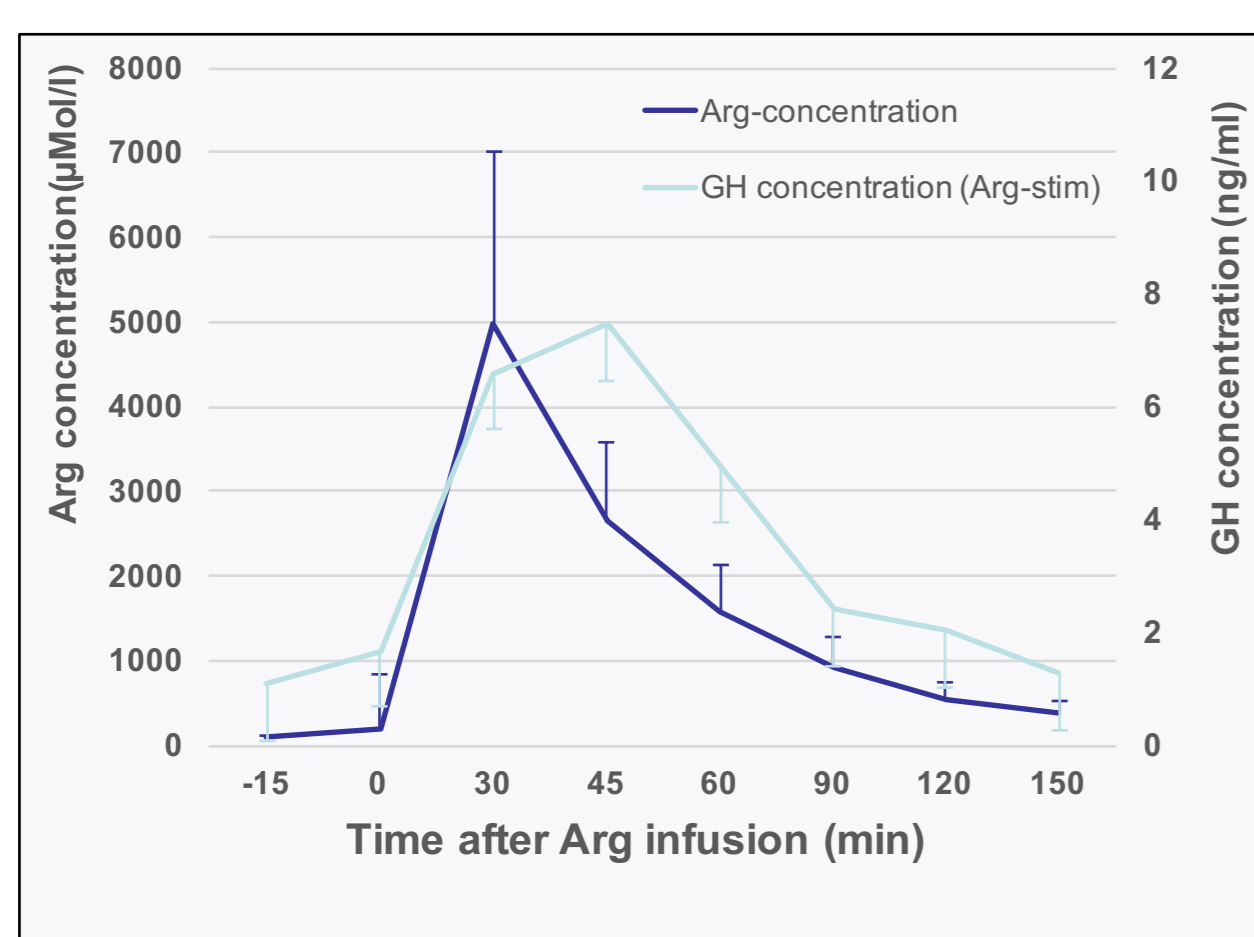
RESULTS

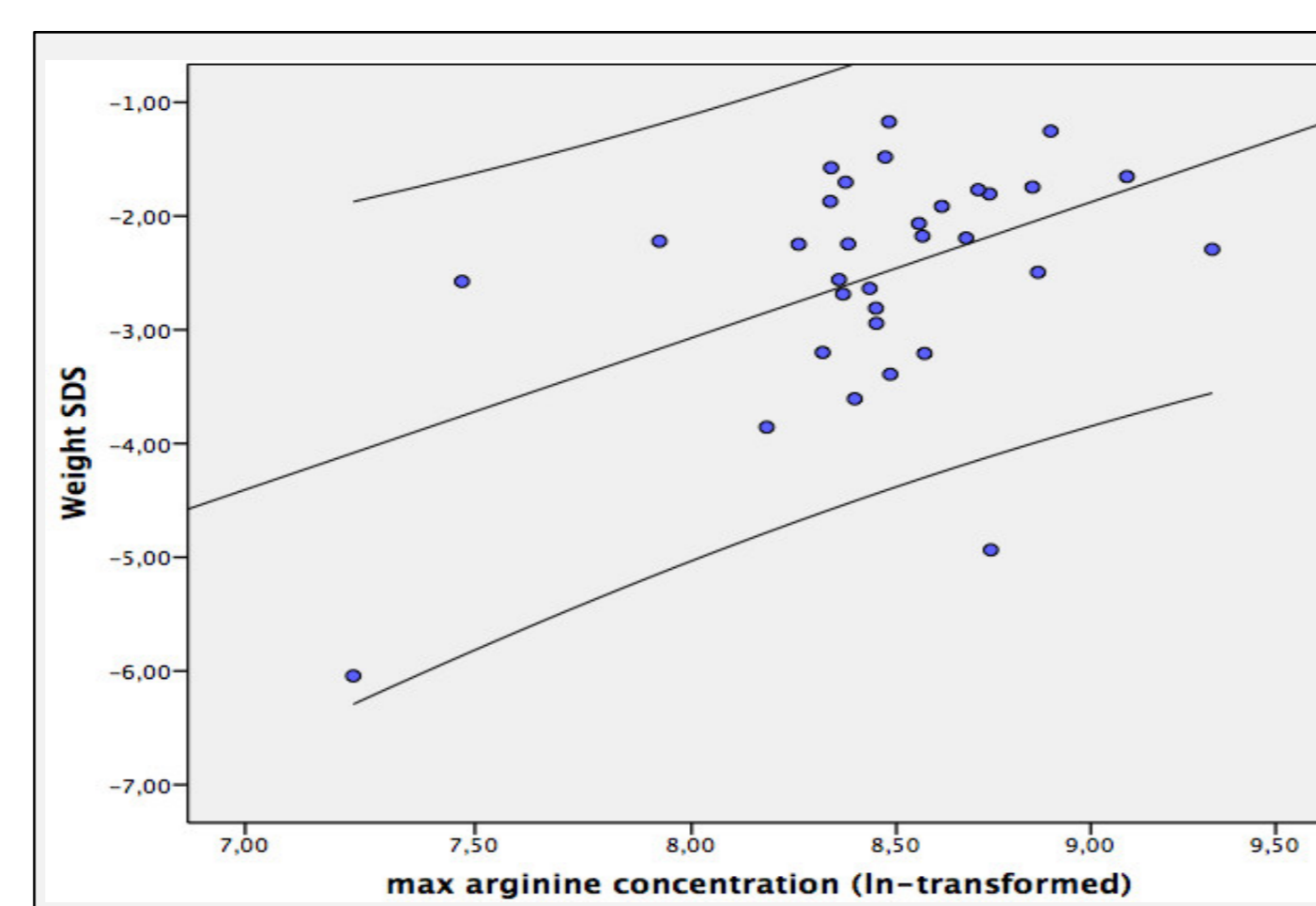Figure 1: Profile of serum Arg and GH concentration after Arg stimulation test

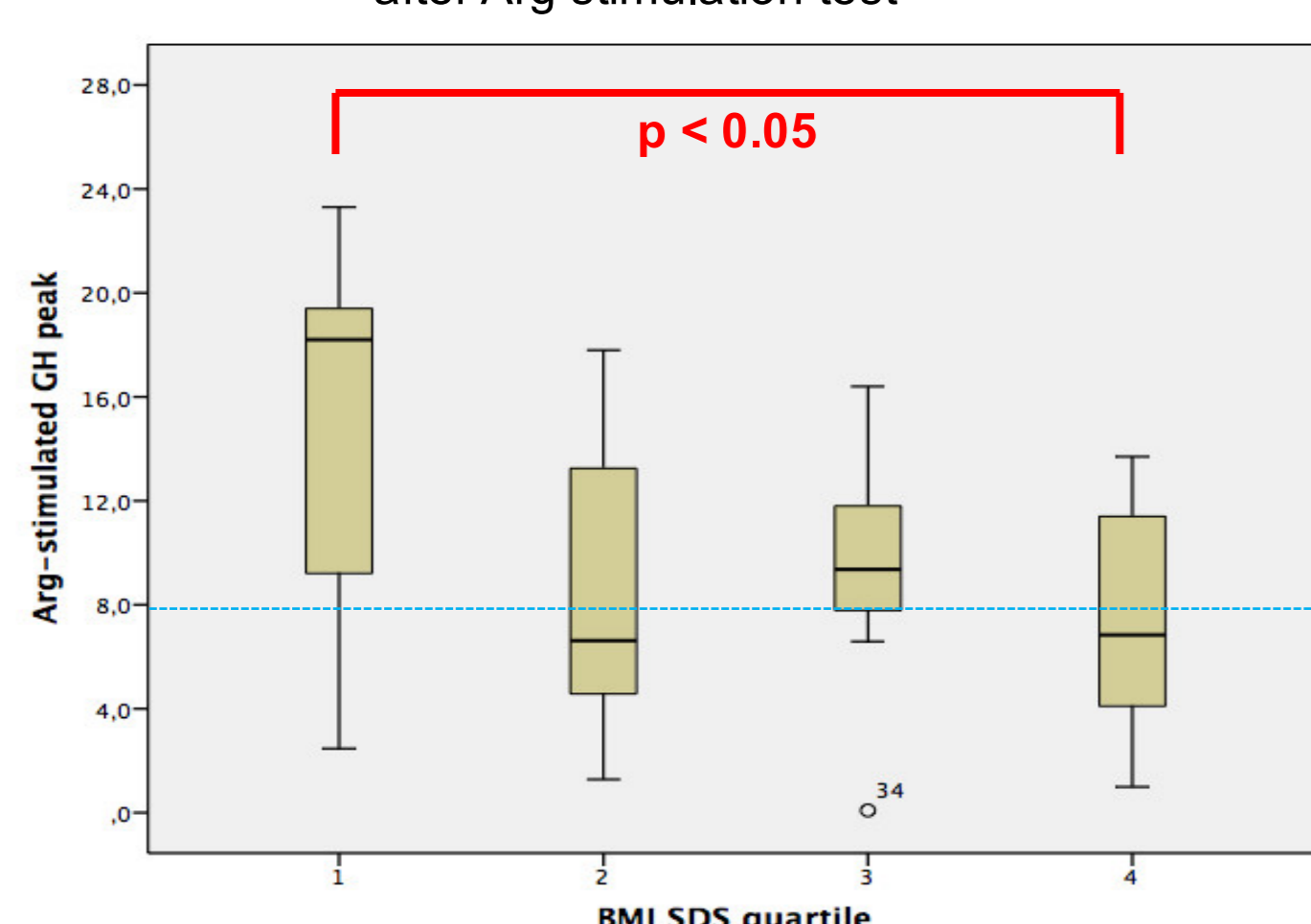Figure 2: correlation of maximal serum Arg concentration and weight SDS

Figure 3: mean Arg-stimulated peak GH concentration in relation to BMI SDS quartile
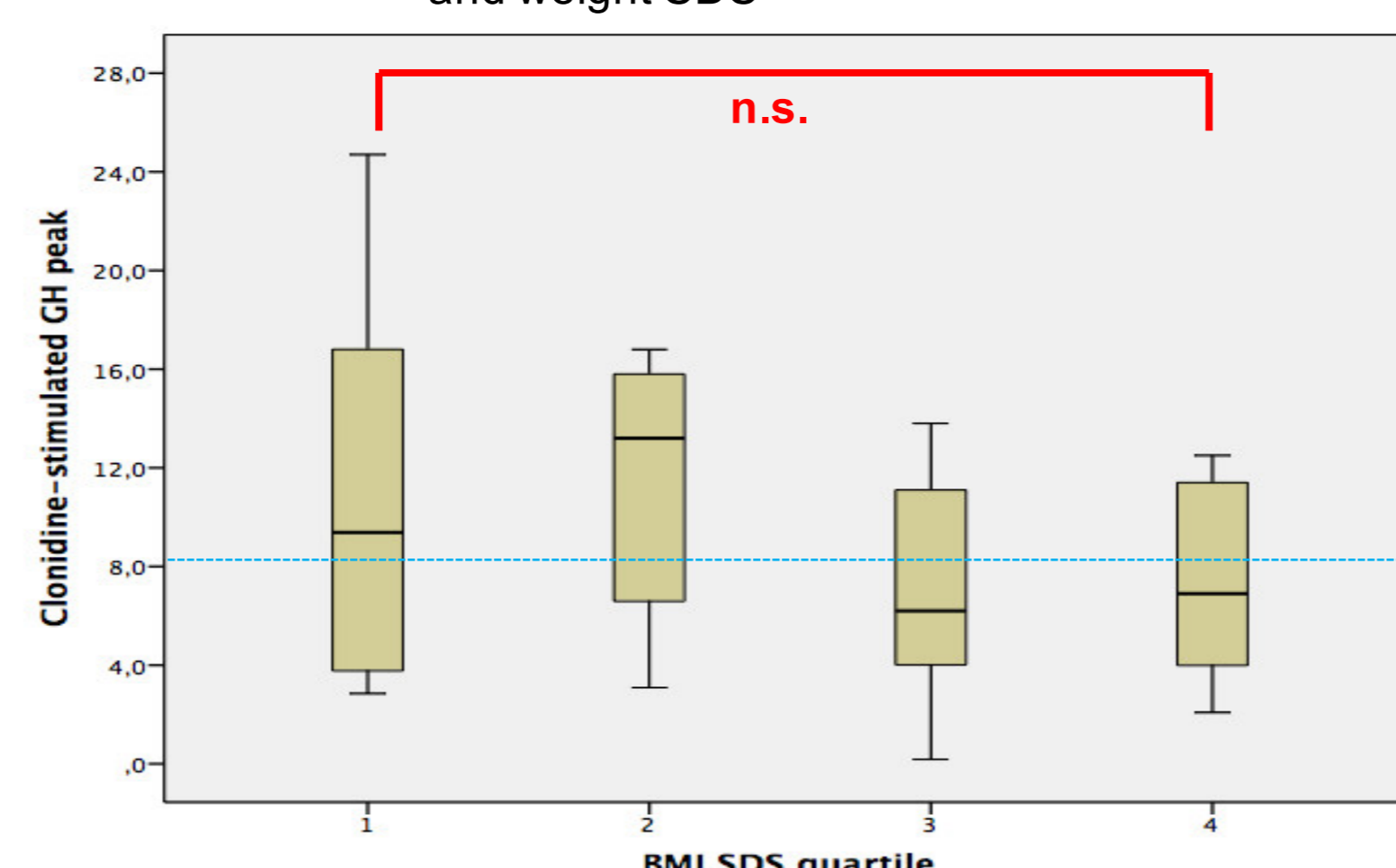

Figure 4: mean Clonidine-stimulated peak GH concentration in relation to BMI SDS quartile

Peak Arg plasma concentrations (4980±364 µMol/l) were observed 30 minutes after start of arginine infusion and preceded peak GH concentration (7.5±1.0 ng/ml) at 45 minutes (figure 1).

Peak Arg plasma concentration correlated both with weight (r=0.464; p<0.01) and height SDS (r=0.407; p<0.05) (see figure 2). We found no direct relation between Arg plasma concentration and Arg-stimulated GH secretion. Furthermore, we found no sex-dependant differences in the Arg plasma concentration profile or Arg-stimulated GH secretion. Peak GH after Arg-stimulation did not correlate with peak GH after clonidine stimulation.

Whereas Arg-stimulated peak GH was significantly higher in the lowest versus the highest BMI quartile, differences in Clonidine-stimulated GH peak did not reach statistical significance (see figure 3 and 4).

In linear regression analyses, weight SDS contributed significantly to the variance of peak Arg concentration (r^2=0.13). Furthermore, BMI SDS contributed significantly to the observed variance in Arg-stimulated peak GH concentration (r^2=0.14).

SUMMARY and CONCLUSIONS

Food intake and energy homeostasis modulate pituitary somatotroph function; in part this seems to be mediated through altering GHRH and somatostatin expression (5). Eating behaviour and associated changes in body composition are therefore likely to interfere with GH stimulation testing in the diagnostic workup of GH deficiency.

In this retrospective study, BMI, weight and height SDS were associated with the arginine plasma profile and the stimulated GH response to arginine stimulation testing. We thus suggest that - as in the diagnostic workup of adults with suspected GHD using Arg+GHRH stimulation testing - auxological parameters such as BMI and weight need further consideration in order to avoid uncontrolled confounding in the interpretation of GH stimulation test results. Preferably this could be achieved by establishing BMI- and/or weight-adjusted reference values in healthy probands.

References

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