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Determinants of advanced bone age in childhood obesity

Introduction

Childhood obesity is associated with advanced bone age (BA), leading to an altered growth pattern. Previous studies suggest that androgens, estrogens, sex hormone binding globulin and insulin are responsible for this phenomenon, but results are contradictory and might be biased by confounders, such as effects caused by aging or progression in to puberty[1-5]. We aim to elucidate this matter by applying a multivariate approach.

Methods

In this cohort study, we performed a correlation analysis of BA standard deviation score (SDS) with androgens, oestrogens and indicators of insulin secretion derived from oral glucose tolerance testing, in a group of obese children and in subgroups according to sex and pubertal status. For oestradiol, testosterone, sex hormone binding globulin (SHBG) and dihydroepiandrosterone sulphate (DHEAS) we calculated age and sex specific SDS using available reference data[6-7] and applying the strategy described by Gerver[8]. An example for DHEAS is shown in figure 1. A multivariate analysis was performed to investigate which parameters were independently predictive of BA SDS.

Results

In this cohort (n=101; 47% female; 56% pubertal; mean age 10.9 yrs; mean BA 11.8 yrs; mean BMI SDS 3.3), BMI SDS was significantly correlated to BA SDS (r=0.55, p< 0.001). In a regression analysis (table 1) in the total cohort (B=0.27, p<0.001), as well as in females (B=0.34, p=0.042), males (B=0.31, p=0.006) and pubertal children (B=0.32, p=0.046), DHEAS showed a positive, independent association with BA SDS. In prepubertal children, SHBG showed an independent negative association with BA SDS (B=-0.41, p=0.013). No association with insulin, insulin resistance or insulin secretion was found.

Conclusions

BMI SDS is highly correlated to BA SDS in obese children. Increased DHEAS is independently associated with advanced bone age in obese children, indicating an independent role for androgen access in advanced bone age in obese children.

Figure 1

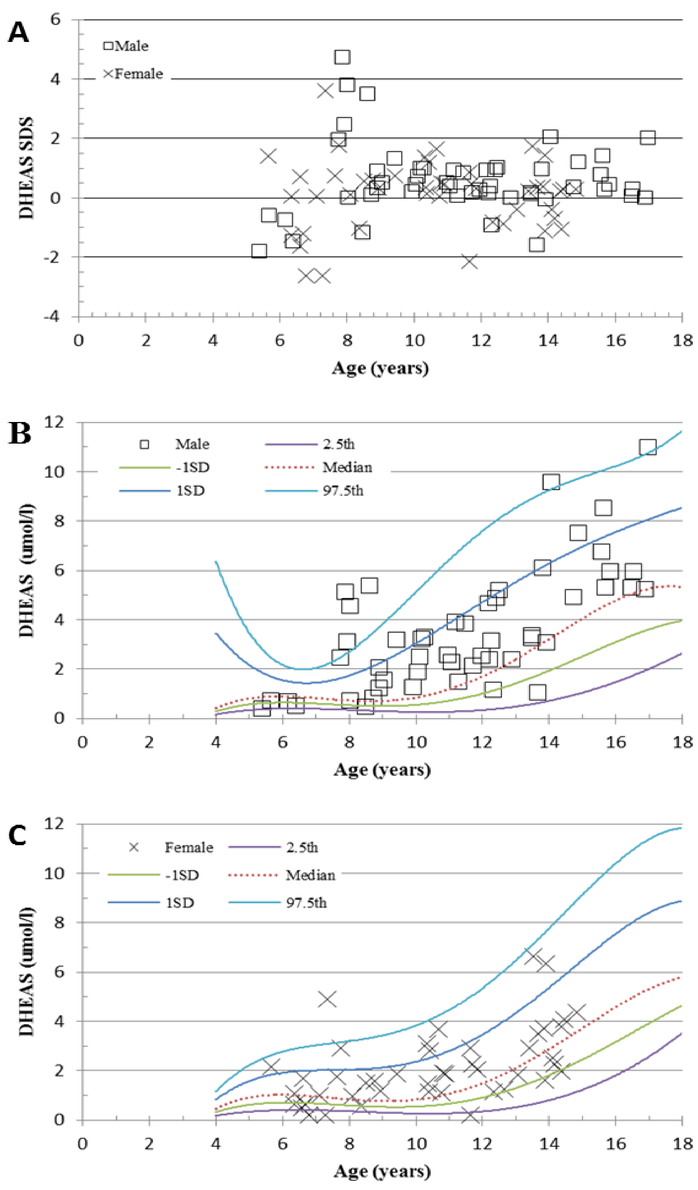

Figure 1 A: Resulting DHEAS SDS for males and females calculated by relating a subjects DHEAS levels to the age specific +1 or -1 SD as shown in figure B and C.

Figure 2

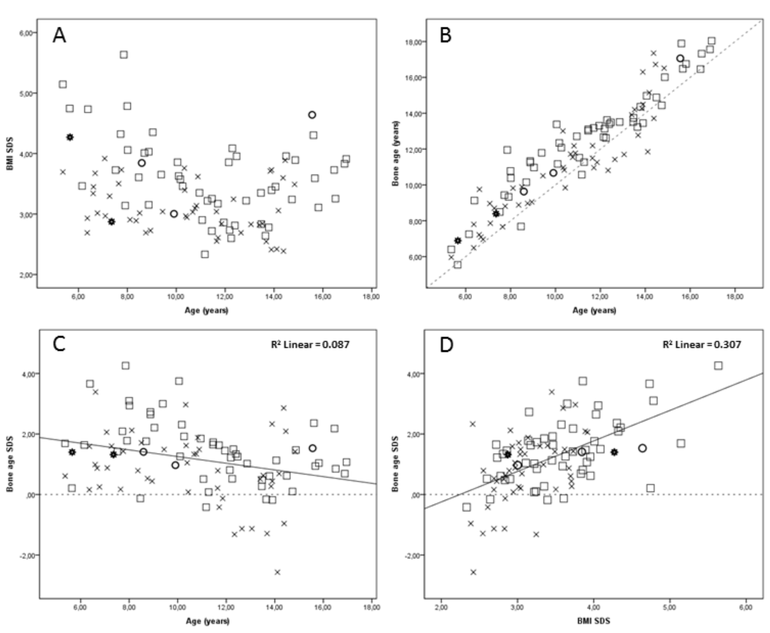

Figure 2 A: representation of BMI SDS and age (years); B: association between bone age (years) and chronological age (years); C: association between bone age SDS and age; D: association between bone age SDS and BMI SDS. Abbreviations: SDS: standard deviation score; BMI: body mass index; R^2: Coefficient of deviation. Squares represent males, x represent females, bold circles represents males with monogenetic obesity, bold stars represent females with monogenetic obesity.

Table 1

		Coefficiënt	CI 95%	R^2	p-value
Total cohort (n=88)	Constant	2.17	1.39/2.96		<0.001
	Sex male	0.62	0.18/1.06		0.006
	DHEAS SDS	0.27	0.09/0.44		<0.001
	Age	-0.13	-0.20/-0.06		0.036
	Model			0.27	<0.001
Female (n=52)	Constant	2.68	1.25/4.11		0.001
	DHEAS SDS	0.34	0.01/0.66		0.042
	SHBG SDS	0.29	-0.04/0.62		0.086
	Age	-0.14	-0.26/-0.02		0.024
	Model			0.21	0.030
Male (n=46)	Constant	2.81	1.80/3.81		<0.001
	DHEAS SDS	0.31	0.09/0.52		0.006
	Age	-0.14	-0.22/-0.05		0.002
	Model			0.30	<0.001
Prepubertal (n=36)	Constant	2.26	1.17/4.02		0.001
	Sex male	0.98	0.30/1.67		0.006
	SHBG SDS	-0.41	-0.76/-0.09		0.013
	Age	-0.27	-0.46/-0.07		0.009
	Model			0.31	0.006
Pubertal (n=37)	Constant	0.70	0.32/1.08		0.001
	DHEAS SDS	0.43	0.01/0.85		0.046
	Model			0.11	0.046

Table 1.Backward linear regression analysis of bone age SDS. Variables included in all model: age, fasting insulin, HOMA-IR, AUC-insulin, DHEAS SDS, SHBG SDS. In the total cohort and pubertal subgroups, sex was added as an independent variable. In the pubertal subgroup only, oestradiol SDS and testosterone SDS were added as independent variables. Abbreviations: HOMA-IR, homeostatic model assessment of insulin-resistance; SHBG, sex hormone binding globulin; DHEAS, Dihydroepiandrosterone sulphate; SDS, standard deviation score.

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