NATURAL ANTIBIOTICS: NEW BIOMARKERS OF CHILDHOOD OBESITY

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BACKGROUND

The innate immune system is one of the first lines of host defense against invading pathogens. Pro-inflammatory α-defensins (mainly DEFA1-3) and anti-inflammatory bacterial/permeability-increasing protein (BPI) are antimicrobial peptides predominantly produced by neutrophils which have been recently related to obesity, type 2 diabetes and cardiovascular risk.

OBJECTIVE AND HYPOTHESES

The aim of our study was to test whether α-defensins and BPI could be new markers of obesity and cardiovascular risk in children.

METHODS

We performed a cross-sectional and longitudinal study in asymptomatic prepubertal Caucasian children.

Plasma α-defensins and BPI (ELISA), body mass index (BMI), waist circumference, systolic blood pressure (SBP), carotid intima media thickness (cIMT), HOMA-IR and HMW-adiponectin were cross-sectionally assessed in 250 children at age 7 years (50% girls, 21% overweight subjects).

α-defensins and BPI were also longitudinally assessed in a subset of these children (n=89) at age ~10 years (49% girls, 0% overweight subjects).

RESULTS

In the cross-sectional study, higher α-defensins concentrations were associated with a poorer cardiometabolic profile, showing positive associations with BMI, waist, SBP, cIMT, HOMA-IR and negative correlations with HMW adiponectin (all between r=0.191 and r=0.377; p<0.01 and p<0.0001). Conversely, higher plasma BPI concentrations were associated with a better cardiometabolic phenotype showing negative associations with BMI, waist, SBP, cIMT, HOMA-IR and positive correlations with HMW adiponectin (all between r= −0.124 and r= −0.329; p<0.05 and p<0.0001).

In the longitudinal study, plasma concentrations of α-defensins, but not of BPI, at age 7 were associated with BMI (β=0.189, p=0.002; model R^2=0.847) and waist (β=0.241, p=0.001; model R^2=0.754) at age ~10 years.

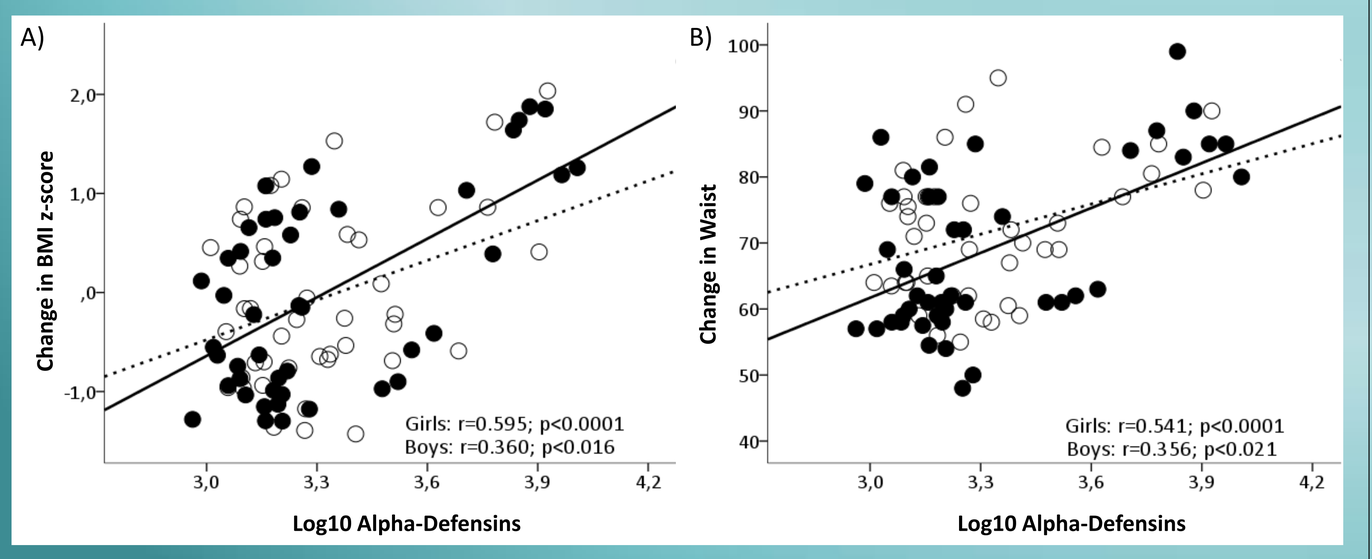

Figure 1: Correlation graphs of α-defensins at ~7 years with A) change in BMI z-score and B) change in waist, at follow-up in the children included in the longitudinal study. Open dots and dashed lines depict boys whereas filled dots and lines depict girls. *r* and *p*-values are shown from Pearson analyses.

Table 1. Clinical and metabolic variables in the study subjects.

	Cross-sectional study	Longitudinal study
Clinical assessments		
N	250	89
Age (y)	7.7 (7.5; 7.9)	10.8 (10.5; 11.0)
Female (%)	49.6	49.4
Puberty (%)	0	47.2
Weight (Kg)	33.3 (31.8; 34.8)	42.1 (39.7; 44.4)
Height (cm)	128 (127; 129)	144 (141; 147)
BMI (Kg/m^2)	19.3 (18.8; 19.8)	19.4 (18.7; 20.1)
BMI z-score	0.6 (0.4; 0.8)	0.5 (-0.1; 0.3)
Waist (cm)	62.8 (61.4; 64.2)	70.4 (68.5; 72.4)
Body fat (%)	33.1 (32.2; 34.0)	32.7 (31.4; 34.1)
SBP (mmHg)	104 (103; 106)	104 (102; 106)
DBP (mmHg)	56 (55; 57)	56 (55; 59)
Carotid IMT (cm)	0.042 (0.040; 0.043)	0.047 (0.046; 0.048)
Metabolic variables		
Glucose (mg/dL)	86 (85; 87)	88 (86; 89)
HDL Cholesterol (mg/dL)	54 (52; 55)	56 (54; 58)
Triacylglycerol (mg/dL)	62 (59; 66)	59 (54; 63)
Insulin (mIU/L)	4.3 (3.8; 4.8)	4.4 (3.6; 5.2)
HOMA-IR	0.94 (0.83; 1.06)	0.97 (0.79; 1.15)
HMW adiponectin (mg/L)	7.3 (6.7; 7.7)	16.6 (12.6; 20.6)
hs-CRP (mg/L)	1.5 (1.3; 1.7)	1.1 (0.8; 1.4)
α-defensins (ng/ml)	2.8 (2.5; 3.2)	--
BPI (ng/ml)	12.3 (9.7; 14.8)	--

CONCLUSION

We suggest that the natural antibiotics α-defensins and BPI may be new markers of childhood obesity. Increased concentrations of α-defensins may predict weight gain and abdominal fat deposition in prepubertal children.