Prenatal pesticide exposure interacts with a common polymorphism in the PON1 gene leading to cardio-metabolic risk profile in childhood.

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Background

Prenatal environmental exposures may influence the risk of developing cardio-metabolic disease later in life. The HDL-associated anti-oxidative enzyme paraoxonase 1 (PON1) protect against atherosclerosis and also hydrolyze environmental chemicals, including organophosphate pesticides. A common polymorphism, *PON1* Q192R, affects both properties. We explored if the PON1 Q192R genotype affects cardiovascular risk factors in school-age children prenatally exposed to pesticides.

Methods

Pregnant women working in greenhouses were categorized as high, medium, or not exposed to pesticides. At age 6 to11 years, their children underwent a standardized physical examination where blood pressure, skin folds, and other anthropometric parameters were measured. Exposure status was unknown to the examiner. PON1-genotype was determined for 141 children. Non-fasting serum was analyzed for IGF-1, IGFBP3, insulin, and leptin.

Table 1. Anthropometric outcomes at school age in children in relation to prenatal pesticide exposure and *PON1* Q192R genotype.

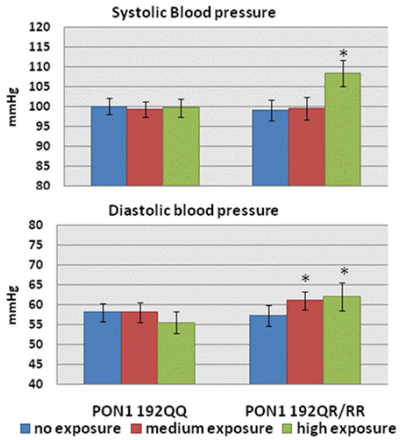
	Geometric mean (95% CI)	
	PON1 192QQ (N=80)	*PON1* 192QR/RR (N=61)
Abdominal circumference (cm)		
No exposure	63.2 (61.0; 65.4)	59.2 (56.8; 61.7)##
Medium exposure	61.0 (58.8; 63.3)	62.4 (60.0; 64.8)
High exposure	62.7 (60.1; 65.4)	65.9 (62.7; 69.3) **
Sum of four skin folds (mm)		
No exposure	43 (38; 49)	34 (30; 39)##
Medium exposure	36 (32; 42)	44 (39; 50) #**
High exposure	44 (38; 51)	52 (44; 62) ***
Body fat percentages (%)		
No exposure	19.1 (17.2; 21.1)	16.0 (14.4; 17.9)#
Medium exposure	16.8 (15.1; 18.7)	19.5 (17.5; 21.6)#**
High exposure	19.6 (17.4; 22.2)	22.3 (19.6; 25.5) ***

Results adjusted for gender, age at examination, social class, and maternal smoking in pregnancy. * p≤0.05 ** p≤0.01 *** p≤0.001 compared to unexposed. # p≤0.05 ## p≤0.01 compared to *PON1* 192QQ in the same exposure group.

Results

An exposure-related increase in abdominal circumference, skin fold thickness, body-fat percentage (Table 1), BMI Z-score, BMI Z-score difference from birth to school age (Table 2), blood pressure (Figure 1), and serum concentrations of leptin and IGF-1 (Figure 2) was seen in children carrying the R-allele. In contrast, children with the PON1 192 QQ genotype showed no significant effect in these outcomes in regard to prenatal pesticide exposure.

Figure 1. Blood pressure at school age in relation to prenatal pesticide exposure and PON1 Q192R genotype.



Bars show geometric mean (95% CI, horizontal lines) adjusted for gender, age, maternal smoking, and BMI. *p<0.05 compared to unexposed

Conclusion

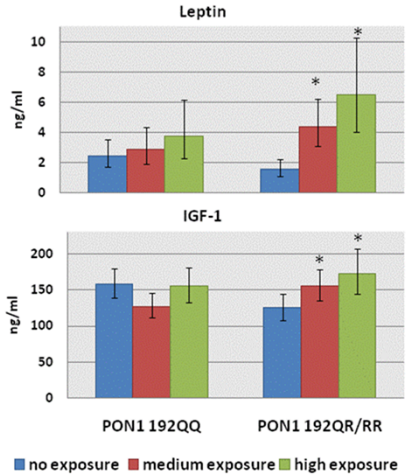
Our results demonstrate a gene-environment interaction between prenatal pesticide exposure and the PON1 genotype that affects cardio-metabolic risk markers already known to be associated with the PON1 192 R-allele. The results also illustrate that a hyper-susceptible subgroup of the population may be more seriously affected, although average effects may not be evident in the entire population.

Table 2. Prenatal pesticide exposure as predictor for BMI Z-scores at school age, and difference in BMI Z-scores between birth and school age in children with the *PON1* 192 QQ or QR/RR genotype.

	Mean difference from unexposed B (95% CI)	
	*PON1*192QQ	*PON1*192QR/RR
BMI Z-score at school age		
Medium exposure	-0.45 (-1.06; 0.15)	0.79 (0.09; 1.50)*
High exposure	-0.07 (-0.73; 0.58)	1.57 (0.76; 2.37)***
ΔBMI Z-score between school age and birth		
Medium exposure	-0.35 (-1.08; 0.39)	1.13 (0.28; 1.99)**
High exposure	0.15 (-0.66; 0.97)	1.29 (0.36; 2.21)**

Results adjusted for social class, maternal smoking in pregnancy and for ΔBMI Z-score also gestational age, * p≤0.05 ** p≤0.01 *** p≤0.001 compared to unexposed.

Figure 2. Non-fasting serum concentrations of leptin and IGF-1 at school age in relation to prenatal pesticide exposure and PON1 Q192R genotype.



Bars show geometric mean (95% CI, horizontal lines) adjusted for gender and age, *p<0.05 compared to unexposed

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