CORRESPONDENCE

FURTHER OBSERVATIONS ON THE RELATIONSHIP BETWEEN ADENOSINE DEAMINASE AND BODY MASS

To the Editor:

We have recently observed in severely obese non–insulin-dependent diabetes mellitus (NIDDM) patients a very high proportion of subjects carrying the ADA*2 allele, suggesting that its presence may favor an increase of body mass.[1] This prompted us to search for confirmatory evidence of such a hypothesis.

The following subjects previously studied by our group have been considered: 365 consecutive newborns from healthy puerperae in the population of Rome, 376 consecutive newborns from healthy puerperae in the population of Penne, 72 nondiabetic obese children in the population of Rome, and 97 newborns from mothers with gestational diabetes (GD) in the population of Rome.

Table 1 shows the proportion of subjects carrying the ADA*2 allele in relation to neonatal macrosomia (defined as percentile weight >90) in newborns from healthy puerperae and in newborns from GD mothers. Table 1 also shows the proportion of subjects carrying the ADA*2 allele in obese children (weight >2 SD). For comparison, the distribution of adenosine deaminase (ADA) in a sample of 982 subjects from the Italian population is also shown.[2]

Table 1. Percent Proportion of ADA*2 Carriers (ADA*1/*2 and ADA*2/*2)

	% Proportion of ADA*2 Carriers	Total No.
1. Control sample	17.1%	982
2. Consecutive newborns from Rome		
2a. Birth weight <90 percentile	16.5%	322
2b. Birth weight >90 percentile	9.3%	43
3. Consecutive newborns from Penne		
3a. Birth weight <90 percentile	17.5%	320
3b. Birth weight >90 percentile	7.1%	56
4. Newborns from mothers with gestational diabetes (Rome)		
4a. Birth weight <90 percentile	10.7%	56
4b. Birth weight >90 percentile	24.4%	41
5. Obese children from Rome Weight >2 SD	8.3%	72

Three-way contingency table anlaysis by a long-linear model

The analysis includes samples 2, 3, and 4 (newborns)

x = ADA genotype
y = birth weight
z = sample

xyz interaction	2 *v* 3 *v* 4	2 *v* 3	(2 + 3) *v* 4	2 *v* 4
	$P < .02$	NS	$P < .01$	$P < .05$

Chi-square test of independence	χ^2	*df*	*P*
All samples	16.633	7	.020
1 *v* 2a *v* 3a *v* 4a	1.683	3	.877
2b *v* 3b *v* 4b *v* 5	8.743	3	.042
(2b + 3b + 5) *v* 4b	5.772	1	.016

NOTE. Newborns are divided into macrosomics (percentile weight > 90) and nonmacrosomics (percentile weight < 90). The weight of nondiabetic obese children is >2 SD.

In nonmacrosomic newborns from healthy puerperae, the proportion of ADA*2 carriers is similar to that observed in the general population. A low proportion of ADA*2 allele carriers is observed in macrosomic newborns from healthy puerperae and in obese children, suggesting a negative effect of ADA*2 allele on body mass increase in absence of diabetes. In newborns from GD mothers, the pattern of association between birth weight and ADA genotype is similar to that observed in NIDDM and opposite to that observed in newborns from healthy puerperae. Thus, the proportion of ADA*2 carriers is much greater in macrosomic infants from GD mother than in macrosomic infants from healthy puerperae.

ADA is a polymorphic enzyme that deaminates irreversibly adenosine to inosine, contributing to the regulation of intracellular and extracellular concentration of adenosine.[3] Since the activity of genotypes carrying ADA*2 allele is lower than that of the most common genotype ADA*1/*1, the concentration of adenosine may be locally higher in ADA*2 carriers than in homozygous ADA*1/*1.

In Zucker rats, an excess of adenosine A1 receptors activity may contribute to adiposity,[4] and our data on NIDDM[1] are in line with the observations in the animal model. The present study suggests that the tendency of ADA*2 carriers to favor body mass increase is characteristic of the diabetic environment.

At least four adenosine receptors have been identified: the physiologic effect of their activation has not yet been fully clarified and may be complex. In some instances, the activation of a receptor class may elicit an effect opposite to that of the activation of another class.[5,6] The relative proportion and activity of adenosine receptors in the metabolic environment of gestational diabetes could be different from those in healthy puerperae, resulting in a diverse effect of low ADA activity on intrauterine growth.

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