

PHENOTYPES OF THE *CHE2* LOCUS OF SERUM CHOLINESTERASE AND ADULT WEIGHT IN A SAMPLE FROM BLUMENAU, SANTA CATARINA, BRAZIL

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ABSTRACT

A sample of 689 blood donors was analysed with the aim of searching for an influence of the *CHE2* locus of serum cholinesterase on adult weight. A frequency of 6.82% of the *CHE2* *CS* + phenotype was observed. The data showed that the distribution of weight is positively correlated with that of serum cholinesterase activity in one phenotype (*CHE2* *CS*-) and independent of it in the other (*CHE2* *CS* +).

INTRODUCTION

Human serum cholinesterase isozymes (acylcholine acylhydrolases, EC 3.1.1.8) are determined by two autosomal nonlinked loci (*CHE1* and *CHE2*). Both loci are polymorphic in most populations already studied (review in Mourant *et al.*, 1976). Considering the *CHE1* locus, the usual allele (*CHE1***U*) is the most frequent (around 95%), the other variants being associated with a decreased activity of serum cholinesterase (ChE) or decreased ability of this enzyme to hydrolyse short-acting muscle relaxants of the succinylcholine type. The *CHE2* locus presents two alleles: *CHE2***CS*- (with frequencies around 95% in the majority of samples investigated) and *CHE2***CS* + . The interaction between the products of the *CHE1* locus and the *CHE2***CS* + allele results in the synthesis of an additional isozyme revealed by

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electrophoretic techniques as an extra band (C₅). The *CHE2**C₅+ allele is dominant over *CHE2**C₅-, the *CHE2* C₅+ phenotype presenting an increased level of ChE activity.

The function of ChE still remains unknown. However, different lines of research have suggested a relationship between fat metabolism and ChE on the basis of data on the activity of this enzyme. Higher activity was found in individuals with a higher weight (Hutchinson *et al.*, 1951; Kalow and Gunn, 1959; Simpson, 1966; Stueber-Odebrecht *et al.*, 1985). A positive correlation between subcutaneous fat and ChE activity was reported by Berry *et al.* (1954). Higher enzyme activity was shown in obese and hyperlipemic subjects (Cucuianu *et al.*, 1968, 1978; Chu *et al.*, 1978). A physical relation between ChE and lipoproteins such as LDL (Lawrence and Melnick, 1961; Dubbs, 1966; Kutty and Acharya, 1972; Kutty *et al.*, 1973, 1975, 1977; Ryhänen *et al.*, 1982) as well as HDL and VHDL (Ryhänen *et al.*, 1982) has been demonstrated. The results suggested that an increase in fat transport is accompanied by an increase in ChE activity.

Considering that the *CHE2* C₅+ phenotype presents an increased level of ChE activity, we decided to investigate whether the variability of the *CHE2* locus had any influence on weight. This interest is justified as previous works had only dealt with enzyme activity with no regard to genetic differences.

MATERIAL AND METHODS

Sera and information on sex, age, race, height and weight were obtained from 689 blood donors. The sample is mainly composed of men (88%), the mean age \pm S.E. is 33.2 ± 0.4 years and the great majority were born (94%) and live (99%) in Santa Catarina, the town of Blumenau being the principal local of birth (55%) and residence (85%). Racial classification, based on skin color, type of hair and facial features showed 86.6% Whites, 1.3% Mulattoes, 1.2% Blacks and 10.9% not classified. More details about the characterization of this sample are reported by Stueber-Odebrecht *et al.* (1985).

The determination of phenotypes of the *CHE2* locus was done according to the method of Robinson *et al.* (1957), as adapted by Van Ros and Vervoort (1973). Results given by the method of Morrow and Motulsky (1968), that distinguishes some phenotypes of the *CHE1* locus, provided a measure of enzyme activity. This measure was taken as the absorbance of the tube without inhibitor.

Statistical analysis was performed with the SPSS and MINITAB computing programs. A search for a possible influence of the *CHE2* locus on weight was based on step-wise multiple regression analysis. Weight was considered as the dependent variable and height, ChE activity, age, sex (0 = male, 1 = female), race (0 = white, 1 = mulatto, 2 = black) and *CHE2* locus (0 = *CHE2* C₅-; 1 = *CHE2* C₅+) were

the independent ones. One analysis considered the whole sample and the two others were done with each class of phenotype.

RESULTS AND DISCUSSION

Table I shows the frequency of the *CHE2* C5+ phenotype obtained in this sample (6.82% \pm 0.96%) as compared with those obtained in other studies. As shown by the χ^2 results, this frequency does not differ from the others.

Table I - Frequencies of the *CHE2* C5+ phenotype obtained in other Brazilian samples, as compared with the frequency estimated in this investigation.

Samples	N	C5+ (%)	χ^2 (P)	References
Blumenau	689	6.82		Present paper
Curitiba	320	4.69	1.724 (> 0.10)	Chautard-Freire-Maia <i>et al.</i> (1984)
Northeast				Ashton and Simpson (1966)
Male	1053	9.31	3.371 (> 0.05)	
Female	1049	6.86	0.001 (> 0.95)	

Table II presents the main results of the three step-wise multiple regression analyses. In the total sample the variables positively correlated with weight were height, age and ChE activity. The regression coefficient given by the *CHE2* locus was not statistically significant, although near the 5% limit. Individuals with higher levels of ChE activity tend to have a higher weight. It is interesting that the group of *CHE2* C5+ phenotypes that show mean ChE activity higher than the *CHE2* C5-, do not show higher weight. Although not statistically different, taken at face values, the mean weight of the group of *CHE2* C5+ individuals is less (70.53 \pm 9.11 kg) than that of the *CHE2* C5- group (72.08 \pm 11.28 kg).

In the sub-sample of the *CHE2* C5+ individuals, weight was positively correlated only with height and age. This result is different from that obtained with the sub-sample of *CHE2* C5- individuals which shows also a positive correlation between weight and ChE activity. The correlation coefficients between weight and this enzyme activity are 0.20 ($P < 0.001$) and 0.06 ($P > 0.70$), respectively, in the *CHE2* C5- and *CHE2* C5+ sub-samples.

The results obtained in the present paper suggest a relation between weight distribution and the genetic variability of the *CHE2* locus. It shows that the distribution of weight is positively correlated with that of serum cholinesterase activity in one phenotype (*CHE2* C5-) and independent of it in the other (*CHE2* C5+). Although the *CHE2* C5+ group showed a higher mean enzyme activity than the *CHE2* C5-

Table II - Results from three step-wise multiple regression analyses, which considered weight (kg) as the dependent variable.

Sample	Mean weight \pm S.D.	a \pm S.E.	F	r ²	Independent variables			t	(P)
						(mean \pm S.D.)	b \pm S.D.		
Total					Height (cm)	170.74 \pm 7.14	0.778 \pm 0.054	14.41	< 0.001
(N = 559) ¹	71.98 \pm 11.15 kg	-79.55 \pm 9.02	74.72	0.35	Age (years)	33.19 \pm 10.17	0.330 \pm 0.038	8.68	< 0.001
					ChE activity	0.79 \pm 0.16	10.003 \pm 2.351	4.25	< 0.001
					CHE2 locus	0.07 \pm 0.25	-2.618 \pm 1.521	1.72	> 0.05
CHE5+	70.53 \pm 9.11 kg	-107.82 \pm 6.48	19.08	0.52	Height	171.47 \pm 5.99	0.96 \pm 0.18	5.33	< 0.001
(N = 38)					Age	32.79 \pm 8.36	0.39 \pm 0.13	3.00	< 0.01
CHE2 C5-	72.08 \pm 11.28 kg	-77.96 \pm 9.17	90.01	0.34	Height	170.69 \pm 7.21	0.768 \pm 0.056	13.71	< 0.001
(N = 521)					Age	33.22 \pm 10.29	0.325 \pm 0.039	8.33	< 0.001
					ChE activity	0.79 \pm 0.16	10.445 \pm 2.455	4.25	< 0.001

¹Only 559 from the sample of 689 individuals presented information on all the variables considered for this analysis.

group, with respective absorbances of 0.858 and 0.787 ($t = 2.83$; $P < 0.01$) it did not present higher weight. Taken at face value its mean weight is even less than that in the *CHE2* C5- group. If this difference in mean weight is real, it may reach a significant level in a sample with a greater number of *CHE2* C5+ individuals.

Many papers had suggested a relation between serum cholinesterase activity and fat metabolism. This relation is reinforced by the present results that indicate an influence of the *CHE2* locus on adult weight, as revealed by the different behaviour of the two phenotypes in terms of correlations between weight and enzyme activity.

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RESUMO

Uma amostra de 689 doadores de sangue foi examinada com o objetivo de se avaliar a relação entre o loco *CHE2* da colinesterase do soro e o peso do adulto. Foi observada uma frequência de 6,82% do fenótipo *CHE2* C5+. Os dados mostraram que a distribuição do peso está positivamente correlacionada com a da atividade da colinesterase do soro em um dos fenótipos (*CHE2* C5-), mostrando-se independente desta no outro (*CHE2* C5+).

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