PRELIMINARY REPORT

Obesity Gene Variant and Elite Endurance Performance

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β_2-adrenergic receptor (*ADRB2*) Gln27Glu genotype was determined in sedentary (n = 19), active (n = 20), and elite endurance athletic (n = 24) Caucasian postmenopausal women. Age was similar in all physical activity and *ADRB2* genotype groups. *ADRB2* genotypes were in Hardy–Weinberg equilibrium in sedentary and active women, but not in the athletes ($\chi^2 = 4.28$, $P < .05$), due to the near absence of *ADRB2* Glu27Glu homozygotes among the athletes. Weight tended to be higher in ADRB2 Glu27Glu women (63.5 ± 1.8 *v* 57.7 ± 1.7 and 60.0 ± 1.8, $P = .08$), as did body mass index (BMI) (25.0 ± 0.4 *v* 22.9 ± 0.6 and 23.4 ± 0.5 kg/m^2, $P = .05$), due to a higher fat mass in Glu27Glu women (24.1 ± 1.0 *v* 18.1 ± 1.4 and 20.1 ± 1.4 kg, $P < .05$). Maximal O_2 consumption was lower in *ADRB2* Glu27Glu than in *ADRB2* Glu27Gln and Gln27Gln genotype women (25.4 ± 1.1 *v* 32.4 ± 1.5 and 29.1 ± 1.7 mL/kg/min, $P < .05$). We conclude that the Glu27Glu *ADRB2* genotype may dissociate from and the Gln27Gln and Gln27Glu genotypes may associate with elite endurance performance in older women.

THE INCREASED FAT MASS of obesity reduces $\dot{V}O_2$max normalized for body weight. Thus, the β_2-adrenergic receptor (*ADRB2*) gene may affect $\dot{V}O_2$max, because functional polymorphisms at *ADRB2* codon 27 influence fat metabolism and susceptibility to obesity.[1-5] We tested the hypothesis that the *ADRB2* Gln27Glu polymorphism associates with endurance performance in women.

MATERIALS AND METHODS

Sixty–three nonobese postmenopausal Caucasian women were recruited into sedentary (n = 19), active (n = 20), and athletic groups (n = 24). Sedentary women had not participated in regular aerobic activity for more than 2 years. Active women participated in aerobic activity for more than 90 min/wk, but did not compete. Athletes were elite competitive distance runners. All were postmenopausal for more than 2 years by self–report, confirmed with elevated luteinizing and follicle-stimulating hormone levels. All had negative exercise electrocardiograms. All subjects signed informed consent approved by the University of Pittsburgh Institutional Review Board.

$\dot{V}O_2$max was measured by open–circuit spirometry and body composition by dual-energy x-ray absorptiometry (Lunar, Madison, WI). *ADRB2* Gln27Glu genotypes were determined by polymerase chain reaction (PCR) amplification.[3] Nonparametric and parametric data were analyzed by Wilcoxon rank–sum and analysis of variance (ANOVA), respectively. Hardy-Weinberg equilibrium was tested using χ^2. Data are reported as mean ± SE.

RESULTS

Age was similar in all physical activity and *ADRB2* genotype groups (Table 1). $\dot{V}O_2$max was highest in athletes and lowest in sedentary women ($P < .0001$). Active women were heavier than sedentary women or athletes ($P < .01$); body mass index (BMI) was lowest in athletes and highest in active women ($P < .0001$). Percent body fat and fat mass were lower in athletes than active or sedentary women ($P < .0001$).

ADRB2 genotypes were in Hardy-Weinberg equilibrium in sedentary and active women (sed, $\chi^2 = 0.63$; act, $\chi^2 = 0.178$; not significant [NS]), but not in athletes ($\chi^2 = 4.28$, $P < .05$) due to the near absence of Glu27Glu homozygotes (Table 2). Weight tended to be higher in Glu27Glu women ($P = .08$), as did BMI ($P = .05$), due to a higher percent body fat and fat mass in Glu27Glu women ($P < .05$). $\dot{V}O_2$max (L/min) was similar between *ADRB2* genotypes (Table 1), but was lower in Glu27Glu women when normalized for body weight ($P < .05$). Adjusting for physical activity group, BMI was still related to *ADRB2* genotype ($P < .05$), and there was an interaction between group and genotype ($P < .05$).

DISCUSSION

Trainability and $\dot{V}O_2$max are genetically controlled, but the specific genes and physiologic phenotypes influencing these traits are largely unknown. Recent findings indicate that *ADRB2* intronic Ban I genotype does not associate with endurance performance in men.[6] However, the present data on the *ADBR2* Gln27Glu locus, which is a missense polymorphism, show that sedentary and active women were in Hardy-Weinberg equilibrium, whereas athletes were underrepresented for Glu27Glu. These conflicting results may be related to functional differences between these loci or to gender differences. The present data suggest a strong disassociation of this genotype from elite endurance athletes and imply that the Glu27Glu *ADBR2* genotype may markedly reduce a woman's chance of becoming an elite distance runner.

ADRB2 regulates fat metabolism and body weight,[1-5] which could well affect the natural selection of endurance athletes, as they generally have low relative fat mass and body weight. Large et al[3] reported that Glu27Glu *ADRB2* women weighed approximately 20 kg more and had 50% larger fat cells than Gln27Gln women, suggesting that Glu27Glu favors fat accumulation. Previous studies have associated Glu27 *ADRB2* al-

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Submitted April 7, 2001; accepted June 25, 2001.

Supported by grants from the Andrus Foundation and the Pennsylvania Heart Association. G.E.M. was supported by NIH Grant No. K08 HL-03029.

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0026-0495/01/5012-0015$35.00/0

doi:10.1053/meta.2001.28140

Table 1. Subject Characteristics by Physical Activity and *ADRB2* Genotype Groups

	PA Groups			*ADRB2* Genotype Groups		
	Sedentary	Active	Athletes	Gln27Gln	Gln27Glu	Glu27Glu
Age (yr)	64 ± 1	63 ± 1	65 ± 1	63 ± 1	65 ± 1	63 ± 2
Weight (kg)	59.2 ± 1.5[b]	64.4 ± 2.0[a]	55.5 ± 1.5[b]	57.7 ± 1.7	60.0 ± 1.8	63.5 ± 1.8
BMI (kg/cm^2)	23.7 ± 0.6[b]	25.2 ± 0.6[c]	21.7 ± 0.4[a]	22.9 ± 0.6[a]	23.4 ± 0.5[a]	25.0 ± 0.4[b]
Body fat (%)	37 ± 1[b]	38 ± 1[b]	25 ± 2[a]	33 ± 2[a]	30 ± 2[a]	38 ± 1[b]
Fat mass (kg)	21.9 ± 1.1[b]	24.3 ± 1.3[b]	14.1 ± 1.2[a]	18.1 ± 1.4[a]	20.1 ± 1.4[a]	24.1 ± 1.0[b]
$\dot{V}O_2$max (L/min)	1.39 ± 0.05[a]	1.70 ± 0.04[b]	2.11 ± 0.06[c]	1.72 ± 0.08	1.85 ± 0.07	1.57 ± 0.09
(mL/kg/min)	23.4 ± 1.1[b]	26.4 ± 0.6[b]	38.0 ± 1.1[a]	32.4 ± 1.5[a]	29.1 ± 1.7[a]	25.4 ± 1.1[b]

NOTE. Values with different superscript letters within the PA or genotype groups are significantly different at $P < .05$.
Abbreviations: PA, physical activity; $\dot{V}O_2$max, maximal O_2 consumption.

Table 2. *ADRB2* Genotype Frequencies by Physical Activity Group

	Genotype		
Group	Gln27Gln (%)	Glu27Gln (%)	Glu27Glu (%)
Sedentary	9 (47)	7 (37)	3 (16)
Active	7 (35)	7 (35)	6 (30)
Athletes	7 (29)	16 (67)	1 (4)

leles with obesity.[1-3,5] In French men, physical activity interacts with the *ADRB2* genotype to counterbalance obesity in the Gln27Gln genotype.[4] Lean women are more likely to be fast runners, so it seems logical that Glu27 homozygotes might be less frequent in our elite athletes. In prior publications, this genotype represented 37% of all women (n = 249) and 23% of nonobese women (n = 101).[2-4] Therefore, approximately 5 to 7 of our athletes were expected to be Glu27Glu. However, whereas the Glu27Glu genotype was present in 23% of our active and sedentary women, it was almost absent from athletes. Moreover, the sedentary and active groups were in Hardy Weinberg equilibrium, but the athletes were not. Thus, our data suggest that *ADRB2* Glu27Glu genotype appears to reduce the likelihood of a woman becoming an elite distance runner.

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