

THE 27GLU POLYMORPHISM OF THE  $\beta_2$ -ADRENERGIC RECEPTOR GENE INTERACTS WITH PHYSICAL ACTIVITY ON OBESITY RISK AMONG FEMALE SUBJECTS.

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Abbreviations: Glu, Glutamate, Gln, Glutamine, METs

Genetic variability in the human  $\beta_2$ -adrenergic receptor (ADRB2) gene could be of major importance for lipolytic function in adipose tissue and also for determining energy expenditure and obesity risk.<sup>1</sup> Furthermore, exercise produces an increase in sympathetic nervous system activity,<sup>2</sup> whose response may be impaired by ADRB2 dysfunction.

In this context, a case-control study was conducted to examine the possible association between obesity risk and the 27Glu polymorphism of the ADRB2 gene depending of physical activity. We screened 252 female Spanish subjects for the 27Glu polymorphism. The serie encompassed 139 obese women with body mass index (BMI) higher than 30 kg/m<sup>2</sup> and no other major disease except for type 2 diabetes, and 113 healthy women with BMI<25 kg/m<sup>2</sup>. Face-to-face interviews together with validated questionnaires were conducted with participants to collect information about their involvement in different physical activities and hours spent sitting down during leisure time. We assigned Metabolic Equivalent (METs) to each activity, obtaining a value of overall weekly METs-hours per participant.<sup>3</sup> The ratio between METs hours/week and the time spent sitting-down during leisure time (M/S) was used to assess recreational energy expenditure. The association between the 27Glu polymorphism and obesity risk

was estimated using multivariate logistic regression. An effect modification (interaction) on the risk of obesity linked to the 27Glu polymorphism by the level of recreational energy expenditure (M/S) was found after adjustment for age (Figure 1). In fact, a statistically significant interaction (product term: M/S x 27Glu allele;  $p=0.005$ ) between recreational energy expenditure and the 27Glu allele was demonstrated (Figure 1).

The average BMI was also compared between the two groups of participants according to energy expenditure using as a cut-off the 75<sup>th</sup> percentile of energy expenditure during leisure time (M/S ratio=0.9). Interestingly, there was a statistically significant interaction in the linear model between the Glu27 allele and the ratio M/S ( $p=0.003$ ). Those women who were more active in their leisure time (M/S>0.9) and were carriers of the 27Glu allele had a higher BMI compared to non-carriers.<sup>4</sup>

Our data reveal that obese women carriers of the 27Glu allele do not benefit equally from physical activity than non carriers, because apparently they are more resistant to lose weight when they expose themselves to higher physical activity levels. The results give an additional perspective to the work of Meirhaegue.<sup>5</sup>

We conclude that the 27Glu allele of the ADRB2 gene appears to be an activity-dependent factor for obesity risk.

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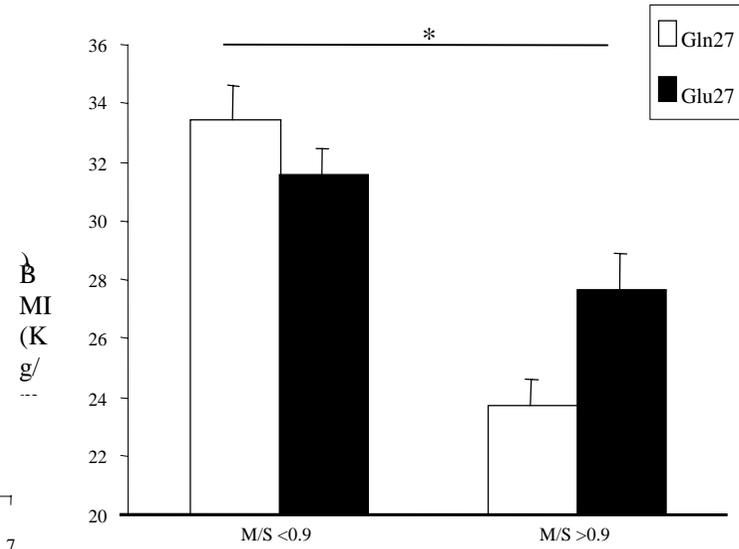
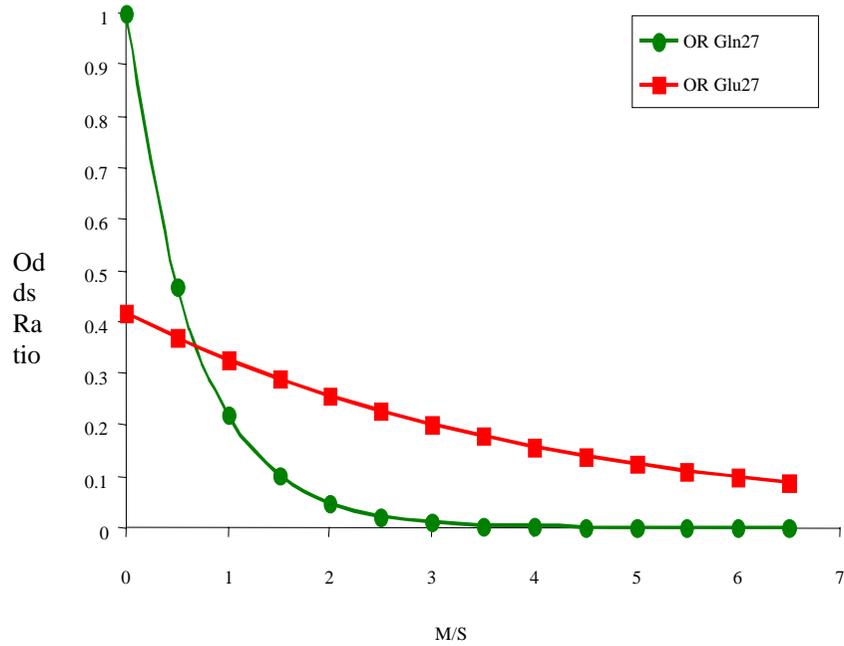
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Figure 1: The change in the magnitude of the association between the Gln27 allele and the obesity risk is dependent of the exposure to physical activity, as it is shown in the left panel where the point estimates for the odds ratio are plotted against the M/S ratio. Average BMI for subjects with (black bars) and without (white bars) the Gln27 polymorphism are seen in the right panel.

The coefficients obtained with the multivariate logistic regression model using obesity (Body Mass Index  $>30$  kg/m<sup>2</sup>) as outcome are shown in the table. They represent independent effects for recreational energy expenditure (M/S), age and the Glu27 polymorphism and a product-term assessing effect modification of the polymorphism by the ratio M/S.

\*  $p < 0.05$

<sup>a</sup> Likelihood ratio test; SE: standard error



	Coefficients	SE	P value <sup>a</sup>
Ratio M/S	-1.52	0.41	<0.001
Age (years)	0.04	0.01	0.007
Glu27 allele	-0.88	0.39	0.024
Product term (M/S x Glu27 allele)	1.28	0.45	0.005