but not in males (Table 3). Compared to carriers of the −2548G allele, female subjects with the A/A genotype had higher age and fat mass adjusted mean plasma concentrations of sOB-R (32.9 ± 7.2 vs. 25.6 ± 3.8 ng/ml, \( P=0.05 \)), and significantly lower (approx. 50%) leptin/sOB-R values (0.74 ± 0.25 vs. 1.42 ± 0.13, \( P=0.02 \)). They also exhibited lower levels of plasma total leptin (approx. 20%), but this difference did not achieve statistical significance (Table 3). The above results were similar when fat mass was substituted for BMI in the statistical analyses, or after adjustment for exercise and smoking status.

To further explore the contribution of the −2548G/A polymorphism in explaining the variation in leptin/sOB-R values, multiple regression analyses were performed, using as independent variables genotype, fat mass and gender. Results revealed that genotype, fat mass and gender are significant and independent predictors of the ratio leptin/sOB-R in this group of healthy Greek subjects, explaining 40% of the variance (Table 4). In additional models, an interaction term involving fat mass and genotype (fat mass x genotype), or gender and genotype (gender x genotype), was introduced to the above multiple regression model, in order to ascertain whether there is an interaction between these factors in predicting free leptin index. We found a significant association of the ratio leptin/sOB-R with the interaction of genotype and fat mass (std beta=0.92, \( P=0.02 \)) in addition to a significant association with gender (std beta=0.38, \( P<0.001 \)). Similarly, in addition to fat mass (std beta=0.43, \( P<0.001 \)), an interaction of genotype and gender in predicting free leptin index (std beta=0.81, \( P=0.03 \)) was observed in the entire study sample. Moreover, the addition of an interaction term explains a higher percentage of variance indicating that an interaction of the factors studied may have physiological significance. In females only, both the −2548G/A genotype (std beta=0.19, \( P=0.02 \)) and fat mass (std beta=0.74, \( P<0.001 \)) are significant predictors of the ratio leptin/sOB-R, explaining 60% of the variance. In contrast, a significant association of leptin/sOB-R with fat mass (std beta=0.40, \( P=0.002 \)) but not genotype (std beta=0.08, \( P=0.52 \)), was observed in males, indicating that this polymorphism does not play a role of comparable importance in men.