The Effect of Dietary Fat on LDL Size Is Influenced by Apolipoprotein E Genotype in Healthy Subjects

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LDL particle size is dependent on both genetic factors and environmental factors such as dietary fat composition. The apolipoprotein E (apoE) genotype is a major genetic determinant of LDL size. Thus, the aim of this work was to study whether the apoE genotype interacts with the quantity and quality of dietary fat, modifying LDL size in young healthy subjects. Healthy subjects (n = 84; 66 apoE 3/3, 8 apoE 4/3, 10 apoE 3/2) were subjected to 3 dietary periods, each lasting 4 wk. The first was an SFA-enriched diet (38% fat, 20% SFA), which was followed by a carbohydrate (CHO)-rich diet (30% fat, < 10% SFA, 55% carbohydrate) or a monounsaturated fatty acid (MUFA) olive oil–rich diet (38% fat, 22% MUFA) following a randomized crossover design. At the end of each diet period, LDL particle size and plasma levels of total cholesterol, LDL cholesterol (LDL-C), HDL-C, apoB, apoA-I, and triacylglycerols were determined. LDL particle size was significantly higher (P < 0.04) in subjects with the apoE 4/3 genotype compared with those with apoE 3/3 and apoE 3/2 in the basal state. LDL size was smaller (P < 0.02) after the CHO diet than after the MUFA or SFA diets. After the CHO diet, a significant increase in LDL particle size (P < 0.035) was noted with respect to the MUFA diet in apoE 4/3 subjects, whereas a significant decrease was observed in the apoE 3/3 individuals (P < 0.043). In conclusion, a Mediterranean diet, high in MUFA-fatty increases LDL particle size compared with a CHO diet, and this effect is dependent of apoE genotypes.
Effect of Apolipoprotein E genotype and saturated fat intake on plasma lipids and myocardial infarction in the Central Valley of Costa Rica.

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We assessed the effect of APOE polymorphisms -491 A/T, C112R (APOE*4), and R158C (APOE*2) and saturated fat intake on plasma lipid levels and risk of myocardial infarction (MI) in 1,927 case subjects and 1,927 population-based control subjects matched for age, sex, and residence, all living in the Central Valley of Costa Rica. A significant gene-diet interaction (p = 0.0157) was observed. High saturated fat intake was associated with a 49% increased risk of MI (OR = 1.49; 95% CI, 1.16-1.92) among wildtype subjects. In contrast, high saturated fat intake was associated with a 2.2-fold increased risk of MI among carriers of APOE*2 (OR = 3.17; 95% CI, 1.58-6.36) and with a 1.6-fold increase among carriers of the -491T and APOE*4 variants together (OR = 2.59; 95% CI, 1.38-4.87). Consistently, a high fat diet elicited a greater response in LDL cholesterol among carriers of APOE*2 (+ 17%) and APOE*4 (+ 14%) compared to noncarriers (+6%). The frequency of APOE variants was similar in case and control subjects, although APOE*4 homozygotes were at increased risk of MI compared to noncarriers (OR = 2.26; 95% CI, 1.03-4.98). This study supports the hypothesis that the APOE*2 and APOE*4 variants increase susceptibility to MI in the presence of high saturated fat and could explain inconsistent findings on the effects of these variants on MI in various populations.
Impact of ApoE genotype on oxidative stress, inflammation and disease risk.

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Although in developing countries an apolipoprotein E4 (apoE4) genotype may offer an evolutionary advantage, as it has been shown to offer protection against certain infectious disease, in Westernised societies it is associated with increased morbidity and mortality, and represents a significant risk factor for cardiovascular disease, late-onset Alzheimer’s disease and other chronic disorders. ApoE is an important modulator of many stages of lipoprotein metabolism and traditionally the increased risk was attributed to higher lipid levels in E4 carriers. However, more recent evidence demonstrates the multifunctional nature of the apoE protein and the fact that the impact of genotype on disease risk may be in large part due to an impact on oxidative status or the immunomodulatory/anti-inflammatory properties of apoE. An increasing number of studies in cell lines, targeted replacement rodents and human volunteers indicate higher oxidative stress and a more pro-inflammatory state associated with the epsilon4 allele. The impact of genotype on the antioxidant and immunomodulatory/anti-inflammatory properties of apoE is the focus of the current review. Furthermore, current information on the impact of environment (diet, exercise, smoking status, alcohol) on apoE genotype-phenotype associations are discussed with a view to identifying particular lifestyle strategies that could be adapted to counteract the ‘at-risk’ E4 genotype.
Apolipoprotein E and lipoprotein lipase gene polymorphisms interaction on the atherogenic combined expression of hypertriglyceridemia and hyperapobetalipoproteinemia phenotypes.


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The combination of hypertriglyceridemia (hyperTG) and hyperapobetalipoproteinemia (hyperapoB) is associated with an increased coronary artery disease (CAD) risk. Apolipoprotein (apo) E and lipoprotein lipase (LPL) genes are involved in the catabolism of triglycerides (TG)-rich apoB-containing lipoproteins (VLDL). SeveralapoE and LPL gene variants affecting CAD risk, plasma TG or apoB concentrations have an allelic frequency of >5% in the general population. This study examined the combined effect of frequent apoE and LPL gene polymorphisms on the expression of hyperTG and hyperapoB. ApoE (E2, E3, and E4) and LPL (D9N, N291S, G188E, and P207L) were genotyped and fasting lipid profiles were assessed among 1,441 French-Canadian subjects. Multivariate analyses were performed to estimate the relationship between apoE and LPL gene variants and the risk of hyperTG (TG>1.7 mmol/l) and hyperapoB (apoB>0.9 g/l). Compared to apoE3 carriers, the apoE4 allele significantly increased the risk of expressing the "hyperTG/hyperapoB" phenotype [odds ratio (OR)=1.95; p=0.014]. This risk was significantly exacerbated (OR=4.69; p=0.017) by the presence of frequent deleterious LPL gene variants in this population. The apoE2 allele was negatively associated with hyperTG/hyperapoB (OR=0.49; p=0.002) in the absence of a deleterious LPL gene variant. These results suggest that epistasis is a phenomenon to consider while assessing the CAD risk associated with gene variants or the effect of frequent alleles on high-risk lipid profiles.
LIPIDGEN APO E

[The role of epsilon 2/epsilon 3/epsilon 4 polymorphism of the apolipoprotein E gene in the development of dislipoproteinemia and its influence on the efficacy of the hypolipidemic therapy]
[Article in Russian]

Vinogradova SV.

Apolipoprotein E (apoE) isoforms have different affinity to lipoprotein (LP) receptors and lipids. In comparison with the "normal" apoE3 the apoE2 affinity to receptors is strictly decreased influencing its association with hypoholesterolemia and accumulation of LP of very-low density in the plasma. The apoE4 is characterized by the increased affinity to LP receptors and is associated with hyperholesterolemia (HCHL). In the homozygotes on allele E2 the gender, age, obesity, diabetes and some other factors have an influence on conversion of hypoholesterolemia to type III hyperlipidemia. The ApoE4 association with HCHL may be due to its impaired recycling in hepatocytes. The ApoE isoforms influence the hypolipidemic therapy efficacy: statins and physical training were more effective in epsilon2 allele carriers and probucol and low-fat diet had the maximal effect in epsilon4 allele carriers.
Alcohol consumption, interleukin-6 and apolipoprotein E genotypes, and concentrations of interleukin-6 and serum amyloid P in older adults.

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BACKGROUND: Whether alcohol intake is associated with concentrations of interleukin-6 (IL-6) and serum amyloid P (SAP) is uncertain. OBJECTIVE: We determined how alcohol intake and apolipoprotein E (apo E) and IL-6 promoter (IL-6-174G-->C) polymorphisms interact for concentrations of IL-6 and SAP. DESIGN: In the Cardiovascular Health Study, 2454 older adults reported their intake of beer, wine, and liquor and underwent measurements of circulating IL-6 and SAP. RESULTS: Alcohol intake was not associated with IL-6 concentrations among apo E4-negative or IL-6C-positive participants but was positively associated among both apo E4-positive and IL-6C-negative participants (P for trend = 0.02 for both). The corresponding interactions on SAP were not significant for alcohol overall but were similar for liquor intake. CONCLUSIONS: Among older adults free of clinical cardiovascular disease, specific IL-6 promoter and apo E alleles appeared to confer positive associations of alcohol consumption with IL-6 concentrations. Genetic heterogeneity should be considered in understanding the cardiovascular effects of alcohol intake.
Apolipoprotein E polymorphism, life stress and self-reported health among older adults.


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OBJECTIVE: To examine the association of self-reported health (SRH) with the apolipoprotein E (APOE) gene, life stress, and sociobehavioural factors in adults aged 55 and over. DESIGN: Secondary analysis of data from the Social Environment and Biomarkers of Aging Study (SEBAS) in Taiwan in 2000, comprising 1023 individuals in 24 communities, using multilevel logistic regression. RESULTS: Allele frequencies are 7.9%, 84.7% and 7.4% for E2, E3 and E4, respectively, similar to those reported in other populations of Asian origins. The apolipoprotein E4 (APOE4) allele was significantly associated with poor SRH overall (odds ratio (OR) 1.54, 95% confidence interval (CI) 1.03 to 2.35), but the association was stronger in women (OR 2.13, 95% CI 1.17 to 3.88) than in men. Individuals who were not satisfied with their living arrangement (OR 3.24, 95% CI 1.99 to 5.29), lived with more than five people in a household (OR 1.52, 95% CI 1.11 to 2.09) or suffered from housing damage in the 1999 earthquake (OR 1.54, 95% CI 0.99 to 2.39) were more likely to report negatively on their health. Individuals who had secondary education (OR 0.52, 95% CI 0.30 to 0.91), often ate vegetables and fruits (OR 0.69, 95% CI 0.5 to 0.94) or exercised often (OR 0.54, 95% CI 0.38 to 0.77) were less likely to negatively rate their health. A significant interaction between the APOE4 allele and physical exercise was found to be associated with SRH. CONCLUSIONS: The APOE4 allele and life-stress factors are associated with SRH, especially in women. Physical exercise is good for health, but benefits may be attenuated among APOE4 allele carriers. This is the first evidence associating a genetic factor and an interaction between APOE4 and physical exercise with SRH. We suggest that well studied genetic factors should be included in health research to control potential heterogeneity.
A Carbohydrate-Rich Diet Reduces LDL Size in QQ Homozygotes for the Gln192Arg Polymorphism of the Paraoxonase 1 Gene


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ABSTRACT: Paraoxonase 1 (PON 1) is an esterase with antioxidant properties that is present in HDL. Gln192Arg polymorphism (also named Q192R or Q/R) of the PON 1 gene that encodes this protein defines two alleles (Q and R). The R allele has been associated with higher cardiovascular risk. LDL size and susceptibility to oxidation also have been identified as cardiovascular risk factors. Our objective was to determine whether genetic variations in the Gln192Arg polymorphism influence LDL size and susceptibility to oxidation after the consumption of diets with different fat content. In our experiments, the participants (n = 98) underwent three 4-wk diets—one, saturated fat-enriched (SAT); another, monounsaturated fat-enriched (MONO); and a third, carbohydrate-enriched (CHO). We observed that LDL were smaller in the QQ group after the CHO diet vs. the SAT (P < 0.01) and MONO diets (P < 0.03). No differences in LDL size were found in QR/RR subjects. When we analyzed lag time of oxidation of LDL, we found that when carriers of the R allele (QR/RR) received the MONO diet, the lag period of LDL oxidation was longer as compared with the CHO diet. Otherwise, we found no differences in QQ homozygotes when we evaluated the lag time of oxidation of LDL after the three diets. These results suggest that the Gln192Arg polymorphism of the paraoxonase gene influences LDL size and susceptibility to oxidation in response to diet.