Butyrylcholinesterase K variant on chromosome 3 q is associated with Type II diabetes in white Caucasian subjects.

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AIMS/HYPOTHESIS: To determine the association of three genes associated with Alzheimer's disease--butyrylcholinesterase (BcHE) on chromosome 3 q, alpha2 macroglobulin (alpha2M) on chromosome 12 p and apolipoprotein E (ApoE) on chromosome 19 q--with Type II (non-insulin-dependent) diabetes mellitus. METHODS: Frequencies of BcHE K variant, alpha2M insertion and/or deletion polymorphism, the ApoE common polymorphisms and promoter variants at ApoE-491 and -291, were examined by fluorescent RFLP in DNA from 276 United Kingdom Prospective Diabetes Study Type II diabetic subjects and 351 non-diabetic subjects from the Diabetes In Families study. Genetic data in diabetic subjects was analysed in relation to clinical characteristics and islet function as assessed by the requirement for insulin therapy 6 years after randomisation. RESULTS: The BcHE K variant allele was more common among Type II diabetic subjects (D) than non-diabetic subjects (ND) (22.8 % D vs 15.8 % ND; p = 0.00 017). Subjects homozygous for the variant were more frequent in the diabetic group (5.8 % D vs 2.6 % ND: p = 0.00 056). The K variant allele frequency was not associated with a requirement for insulin therapy (29.0 % insulin-requiring vs 21.8 % non-insulin-requiring; p = 0.121). There were no associations of alpha2M and ApoE polymorphisms or ApoE promoter variants with clinical characteristics or insulin requirement in diabetic subjects. There were differences in total cholesterol (p = 0.0005) and LDL-cholesterol (p = 0.0009) among non-diabetic subjects in relation to ApoE-491 genotypes. CONCLUSION/INTERPRETATION: The association of the BcHE gene (3q26) with Type II diabetes could be related to an identified susceptibility locus on chromosome 3q27 but appears to be independent of islet function. The absence of diabetes-specific associations with alpha2M, ApoE or ApoE promoter variants suggest that these are not important in the onset of hyperglycaemia.