Alpha-1-antitrypsin and blood pressure

SIR,—Alpha-1-antitrypsin (AAT) inhibits a wide range of proteases including trypsin, thrombin, and elastase. In man, AAT is encoded by the highly polymorphic protease inhibitor (PI) locus. The M subtype alleles are most common with a combined frequency of about 0·95. The two most common deficiency alleles are S and Z, with frequencies of around 0·03 and 0·02, respectively. These alleles lead to reductions in serum AAT concentrations, and are associated with lung and liver disease.[1]

In a Dutch study of cardiovascular risk factors in 160 twin pairs (aged 14–20 years) and their parents,[2] we examined the relation between PI type and blood pressure, which was measured during both rest and tests of reaction time and speeded mental arithmetic. 44 parents of twins had at least one S or Z allele. 34 subjects were excluded because they were receiving medication that might influence blood pressure (including oral contraceptives). Among fathers (mean age 48 years), non-MM types had significantly lower systolic blood pressure (SBP) than MM types ($p = 0·008$), and there was a significant interaction between PI and the tests of reaction time and mental arithmetic ($p = 0·021$), indicating a greater reactivity of MM types to stress (figure). For diastolic blood pressure (DBP), the effect of PI type was not significant ($p = 0·069$), and there was no interaction with the tests. Differences in mothers (mean age 46 years) and twin offspring (mean age 16·7 years) were also non-significant. Since these associations could be the result of type I errors, we investigated the relation of PI type and blood pressure in an earlier study of ethanol sensitivity in Australian twins.[3] PI phenotype was available for 316 healthy subjects aged 18–34 years (mean age 23).[4] Blood pressure was taken after subjects had rested for 2 min in a supine position. The first measure was taken before alcohol intake and then at 1, 2, and 3 h after ingestion of a standard dose of alcohol. 25 males and 35 females had deficiency alleles. Once again, we found a significant difference in systolic blood pressure between MM and non-MM males ($p = 0·011$). Differences for DBP and for females were not significant.

The lower SBP of 7–8 mm Hg observed in both Dutch and Australian males carrying PI deficiency alleles may help to offset some of the adverse effects of AAT deficiency. A likely mechanism is the reduced inhibition of elastase which attacks elastin in arterial walls. A further consequence of this effect is the increased risk of abdominal aortic aneurysm in PI Z carriers.[5] In addition, studies in animals have shown that elastase lowers blood pressure.[6] Since 10–20% of Europeans carry PI S or Z alleles, it is important to investigate whether PI type interacts with other environmental and genetic risk factors affecting blood pressure.

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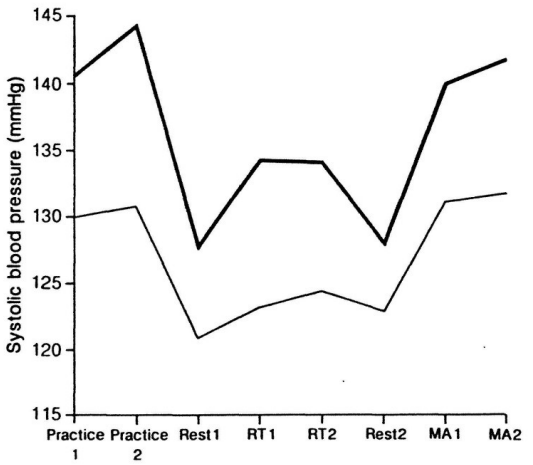

Systolic blood pressure during rest and test conditions.

RT = reaction time; MA = mental arithmetic. ——, MM genotype; ——, non-MM genotype.