

A POLYMORPHISM IN THE Ah-RECEPTOR GENE IS RELATED TO HYPERTENSION IN MIDDLE-AGED MEN

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Abstract

Exposure to the dioxin-like compound PCB 126 (3,3',4,4',5-pentachlorobiphenyl) increased blood pressure in rats. Humans living in areas contaminated with persistent organic pollutants (POPs) showed an increased prevalence of hypertension. Dioxin-like POPs act through the dioxin receptor (Ah-receptor). The aim of the present study was to investigate if single nucleotide polymorphisms (SNP) in the Ah-receptor gene are associated with hypertension in humans.

In a cohort of men in Uppsala, Sweden, blood pressure was measured at the age of 50. Four SNPs in the Ah-receptor gene was determined by a minisequencing system in 976 subjects. Compared with the subjects being homozygote for the C allele (CC, n=22) in one of the SNPs (rs 4519497), carriers of one (n= 129, odds ratio 3.77, 95%CI 1.09-13.1, p= 0.036) or two T alleles (n=825, odds ratio 3.60, 95%CI 1.06-12.3, p= 0.040) showed significantly increased prevalence of hypertension.

A polymorphism in the Ah-receptor gene was found to be protective for hypertension in middle-aged males. This finding is consistent with the view that the Ah-receptor is involved in the regulation of blood pressure.

Introduction

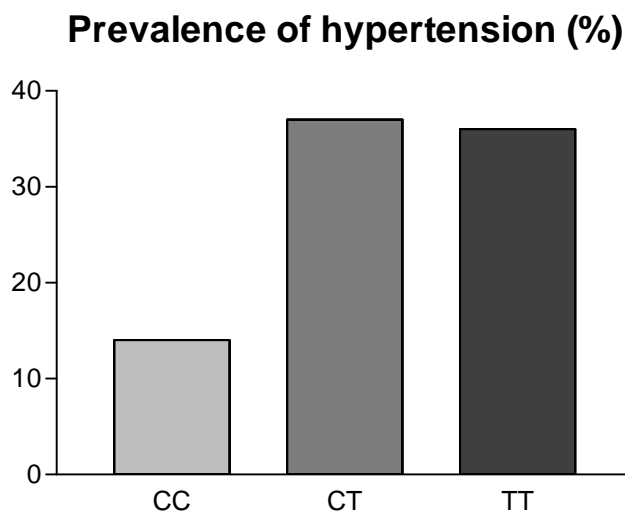
We have recently shown that exposure to the dioxin-like compound PCB 126 (3,3',4,4',5-pentachlorobiphenyl) resulted in increased blood pressure in rats¹. In addition, recent epidemiological studies in subjects living in areas contaminated with persistent organic pollutants (POP) suggest that exposure to persistent organic pollutants such as organochlorines, result in both an increased prevalence of hypertension and an increased risk of cardiovascular diseases^{2,3}. POPs, which are dioxin-like compounds, act through the dioxin receptor (Ah-receptor). The aim of the present study was to investigate if single nucleotide polymorphisms (SNP) in the Ah-receptor are associated with hypertension in humans.

Material and Methods

In a population-based cohort of middle-aged men (The Uppsala Longitudinal Study of Adult Men, ULSAM) in Uppsala, Sweden⁴, blood pressure was measured at the age of 50. Hypertension was defined as blood pressure >140/90 mmHg or antihypertensive medication. Four SNPs in the Ah-receptor gene was determined by a minisequencing system in 976 subjects in the ULSAM cohort.

Results and Discussion

Compared with the subjects being homozygote for the C allele (CC, n=22) in one of the SNPs (rs 4519497), carriers of one (n= 129, odds ratio 3.77, 95%CI 1.09-13.1, p= 0.036) or two T alleles (n=825, odds ratio 3.60, 95%CI 1.06-12.3, p= 0.040) showed significantly increased prevalence of hypertension.



A polymorphism in the Ah-receptor was found to be protective for hypertension in middle-aged males. This finding is consistent with the view that the Ah-receptor is involved in the regulation of blood pressure and indicates a possible mechanism whereby exposure to POPs could influence blood pressure in both the experimental setting and in humans.

References

1. Lind PM, Orberg J, Edlund UB, Sjoblom L, Lind L. *Toxicol Lett* 2004; 150:293.
2. Huang X, Lessner L, Carpenter DO. *Environ Res* 2006; 102:101.
3. Shcherbatykh I, Huang X, Lessner L, Carpenter DO. *Environ Health* 2005. 4:18.
4. Ingelsson E, Sundstrom J, Arnlov J, Zethelius B, Lind L. *JAMA* 2005; 294:334