
Metabolic Aspects and Mechanisms

9.22 A Human Fatty Acid Amide Hydrolase (FAAH) Functional Gene Variant Is Associated with Lower Blood Pressure in Young Males

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Introduction. Fatty acid amide hydrolase (FAAH) inhibitors, preventing endocannabinoid (EC) degradation, reduce blood pressure (BP) and heart rate in young male hypertensive rodents. The functional human FAAH 129T gene variant results in reduced protein level and enzymatic activity but its relationship with BP is unknown. This study investigates the relationship among FAAH P129T alleles and cardiovascular features in young males (YM) at baseline and after 9-year follow-up, and in older male obese hypertensive (OH) patients, in whom the endocannabinoid system (ECS) is overactive.

Methods. Genotype analysis was performed in 215 Caucasian YM [mean age 24 (0.2) years] participants of the Ancona Heart Doctor Study and in 185 male OH patients [mean age 50 (0.2) years]. YMs were also followed up for 9 years. Clinical and anthropometric variables, BP, cardiac and carotid artery echographic measurements were evaluated.

Results. YMs with the FAAH 129T allele had lower systolic (125.5 vs. 129.5 mmHg, $p=0.042$) and mean BP (94.1 vs. 97 mmHg, $p=0.022$), and a trend toward lower diastolic BP (78.4 vs. 80.8 mmHg, $p=0.06$). Such significant association was maintained at follow-up (SBP115.9 vs. 121.1 mmHg, $p=0.024$; MBP 90.3 vs. 93.8 mmHg, $p=0.022$; DBP 80.1 vs. 77.6 mmHg, $p=0.08$). In contrast, the same allele was not associated with BP in older OH. No association was found with other cardiac and vascular variables.

Conclusions. An FAAH defective gene variant results in lower BP in YMs, similarly to the findings in young rodents. This effect is lost in older OH patients. Because cannabinoid CB1 receptor blockade with rimonabant is associated with BP reduction in OH patients, EC effects and the use of ECS-interfering drugs is likely to be age and clinical condition dependent.