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Polymorphism of the α-2a adrenoreceptor gene and aerobic power in coronary artery disease

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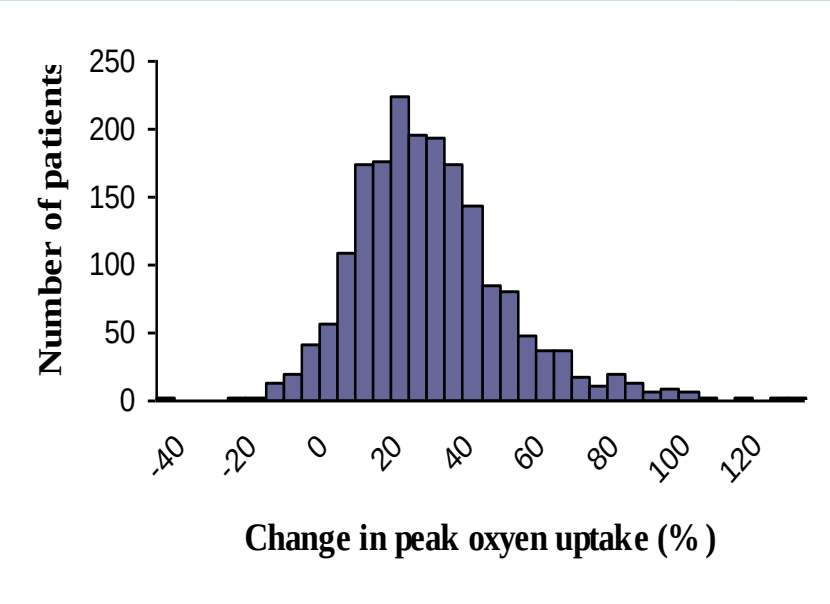
Variation in change of exercise capacity



- Age
- Gender
- Training frequency
- Training intensity
- Baseline exercise duration
- …

Explanation of 20pct of variation

Vanhees et al. Eur J Cardiovasc Prev Rehabil 2004,11:304-312

The Caregene study

CArdiac REhabilitation and GENetics of Exercise performance and training effect

Aim:

To explore the effect of genetic variation on aerobic power and on the response to physical training in patients with coronary artery disease

Inclusion criteria:

Men or women
Biologically unrelated
AMI and/or PCI a/o CABG a/o AP, but not artificial valve or heart transplantation or ICD or other cardiac surgery
Evident exhaustion during both graded exercise tests

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Exercise training

- Cycling, running, arm ergometry, rowing, predominantly dynamic calisthenics and relaxation
- Duration: approximately 100 minutes/session
- Frequency: 3 exercise sessions weekly during 3 months

  2.27 ± 0.47 sessions per week
- Intensity: $HR_{training} = HR_{rest} + 60\% - 90\% (HR_{peak} - HR_{rest})$

  $79.7 \pm 10.4\%$

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Clinical characteristics

- Men/Women: 839/76 (92%/8%)
- Age: 56.3 ± 9.23

- AMI: 630 (67%)
- CBG: 377 (40%)
- PCI: 470 (50%)
- Angina: 23(2%)

- β-blockers: 794(85%)
- Converting enzyme Inhibitors: 222(24%)
- Antiplatelets: 829(89%)

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Candidate genes

Renin Angiotensin Aldosteron System

ACE gene (insertion/deletion)

Angiotensin II type 1 receptor gene

Vascular and endothelial function

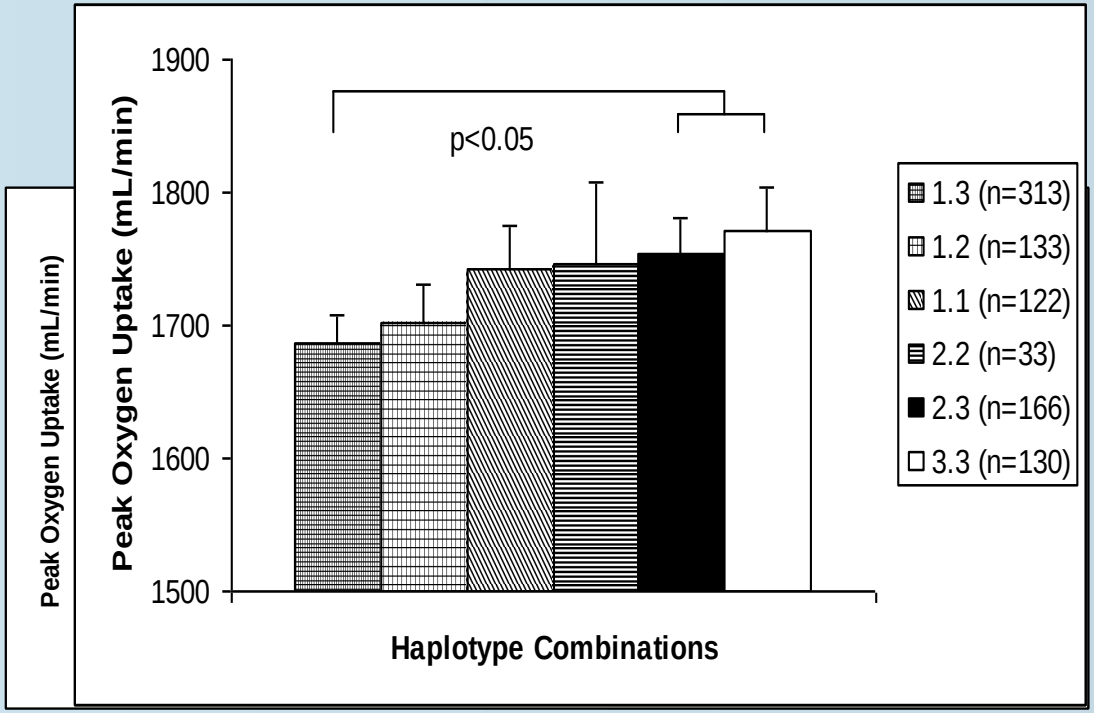
eNos (NOS3) gene

α-2a-adrenoreceptor gene

Adrenergic function

β1- adrenoreceptor gene

β2- adrenoreceptor gene



The Caregene study

Polymorphism of the α2a-AR gene: background

- Presynaptic inhibitory autoreceptor:
  - blood pressure, heart rate
- α2a-AR gene:
  - chromosome 10 (q24-q26)
- DraI Restriction fragment length Polymorphism in the α2a-AR gene (Hoehe 1988)*:
  - a two-allele polymorphism with bands at 6.7kb (wild type) and 6.3kb (mutation)
- DraI RFLP polymorphism in the α2a-AR gene associated with elite endurance athlete status (Wolfarth 2000)**

* Hoehe MR, Berrettini WH, Lentes KU. Nucleic Acids Res. 1988 Sep 26;16(18):9070.

** Wolfarth B,Rivera MA, Oppert JM et al.Med Sci Sports Exerc. 2000 Oct;32(10):1709-12.

The CAREGENE study

Polymorphism of the α2a-AR gene: distribution

Genotype distribution in our population:

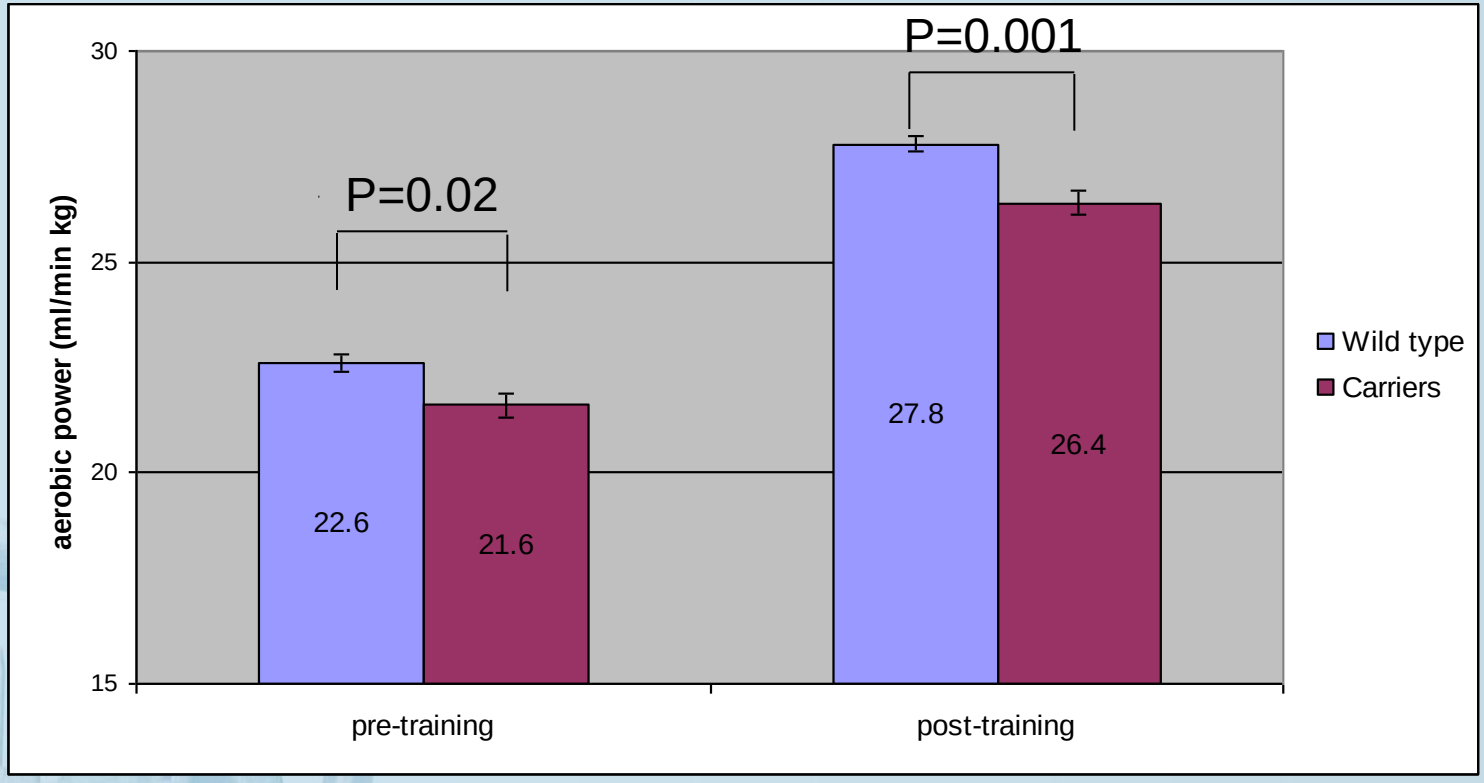
- 915 were succesfully genotyped:
  - 622 (68 %) homozygous wild-type (6.7kb/6.7Kb) → Wild-type
  - 267 (29%) heterozygous (6.7kb/6.3kb)
  - 26 (3%) homozygous mutant-type (6.3kb/ 6.3kb)

  → Carriers

- Genotype distributions were in agreement with the prediction by Hardy-Weinberg equilibrium ($p<0.05$)

The Caregene study

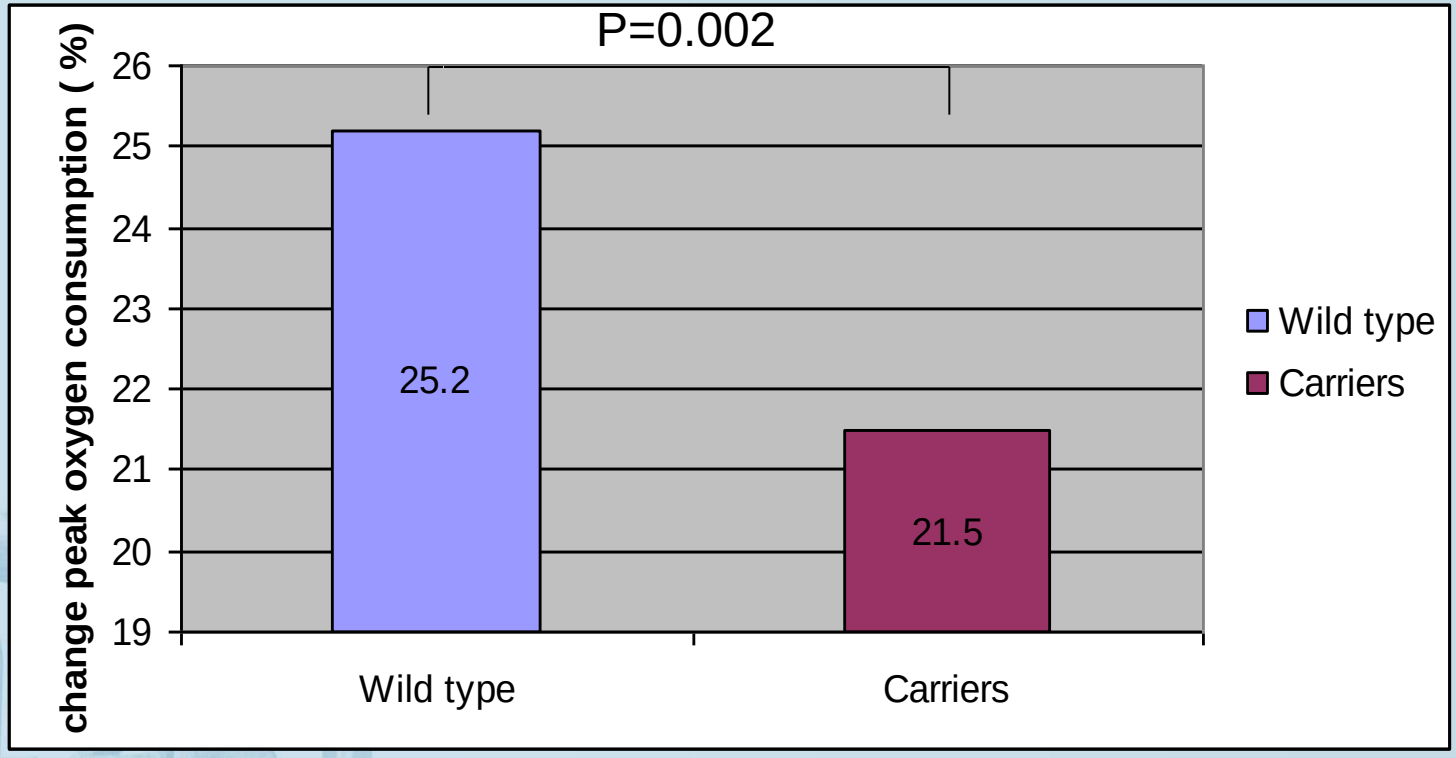
α2a -AR gene: Aerobic power



Data are presented as means. Comparisons between groups were made by means of ANCOVA. Adjusted for age, sex and height.

The Caregene study

α2a -AR gene : Aerobic power response



Data are presented as means. Comparisons between groups were made by means of ANCOVA. Adjusted for age, sex, height, baseline aerobic power, training intensity and frequency

The Caregene study

α2a -AR gene : Conclusion

- In Caucasian patients with CAD of the CAREGENE study
  - Associated with aerobic power at baseline and after training
  - Strong association with the response to training: additional increase of 4%
- Additional explanation of 0.8 % of the variation of change in exercise capacity

Questions ?

Thank you for your attention