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

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
  \[2.27 \pm 0.47 \text{ sessions per week}\]
- Intensity: \( HR_{\text{training}} = HR_{\text{rest}} + 60\% - 90\% \ (HR_{\text{peak}} - HR_{\text{rest}}) \)
  \[79.7 \pm 10.4\%\]
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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

**Adrenergic function**
β1- adrenoreceptor gene
β2- adrenoreceptor gene

α-2a-adrenoreceptor gene

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**Peak Oxygen Uptake (mL/min)**

- Ser49-Gly389/Ser49-Gly389 (n=45)
- Ser49-Arg389/Ser49-Gly389 (n=243)
- Ser49-Arg389/Ser49-Arg389 (n=245)
- Ser49-Gly389/Gly49-Gly389 (n=11)
- Ser49-Gly389/Gly49-Arg389 (n=129)
- Ser49-Arg389/Gly49-Arg389 (n=173)
- Gly49-Arg389/Gly49-Arg389 (n=16)

**p=0.003**
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Polymorphism of the α2a-AR gene: background

- Presynaptic inhibitory autoreceptor:
  - blood pressure, heart rate
- α2a-AR gene:
  - chromosome 10 (q24-q26)
- Dral 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)
- Dral RFLP polymorphism in the α2a-AR gene associated with elite endurance athlete status (Wolfarth 2000)**

The CAREGENE study
Polymorphism of the α2a-AR gene: distribution

Genotype distribution in our population:

• 915 were successfully 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)
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.
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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