Gender differences in AMPK activation in the heart and white quadriceps muscle following exercise training in mice.

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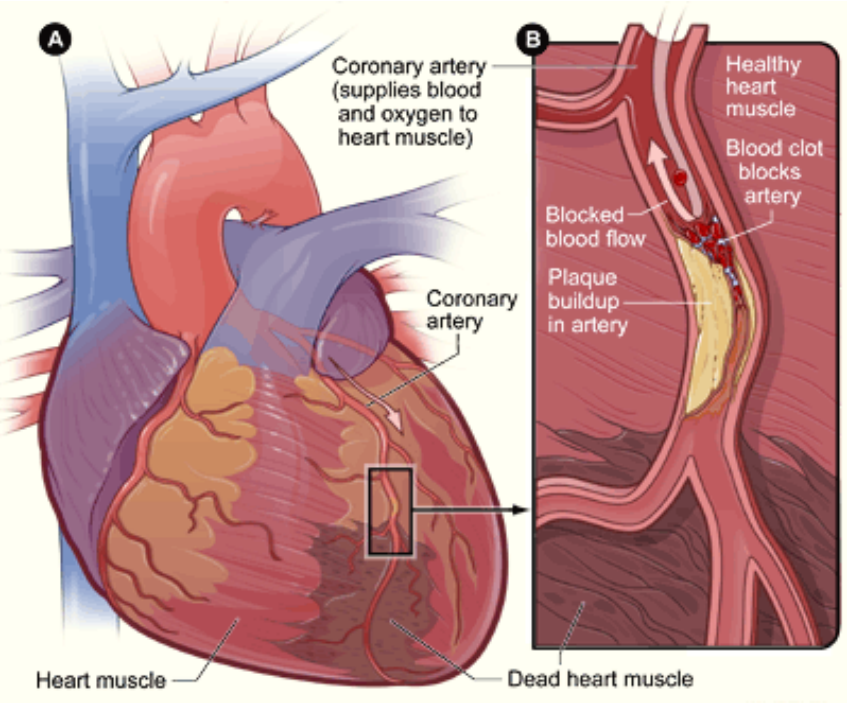
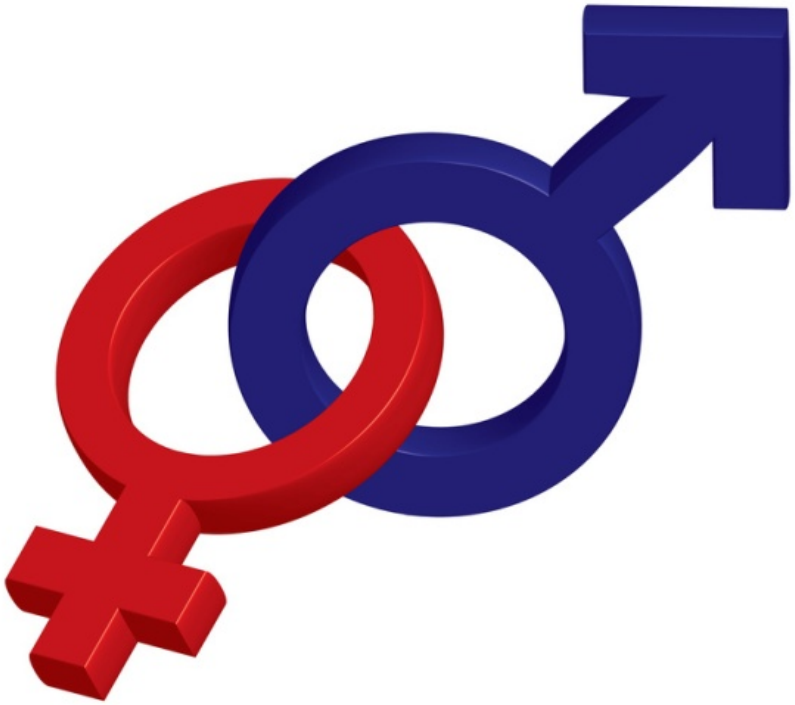
Ischemic Heart Disease



#1 cause of death in the USA
(9)

Introduction: Application



- Optimal cardiac treatment

Introduction: Differences and K_{ATP} channels

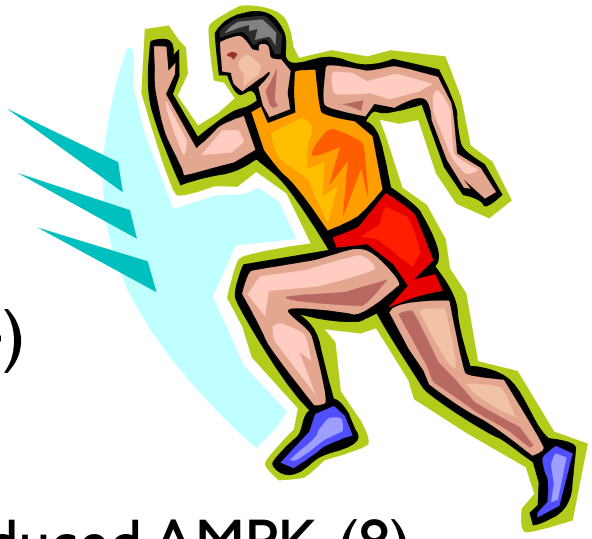
- Infarct size post-MI (rats)
  - Female<Male
- ATP-sensitive potassium (K_{ATP}) channels
  - Female>Male
- Blocking K_{ATP} channels
  - Males: infarct size unaffected
  - Females: infarct size modulated (3)
- So where does MALE cardio-protection come from?

Introduction: AMPK

- Myocardial AMPK activation=critical to tissue-preserving response during ischemia
  - AICAR 24 hours prior to MI
    - 60% reduction in murine infarct size.
  - ATP-consuming pathways ⬇
  - ATP-generating pathways ⬆

Introduction: AMPK and Exercise

- Exercise 24 hours prior=Protective (5)
- ↑exercise=↑AMPK activation (4)
- Exercise training → ↑exercise-induced AMPK (8)



Introduction: Differences and AMPK

- Human Skeletal Muscle
  - Men=210% increase in AMPK activity immediately post-exercise
  - Women= no significant difference in AMPK activity (6)

- Is there a similar effect in the heart?

Purpose

- to investigate whether a gender difference exists in the heart's ability to activate AMPK a

AND

- Is the difference observed modulated by exercise training?

Methods

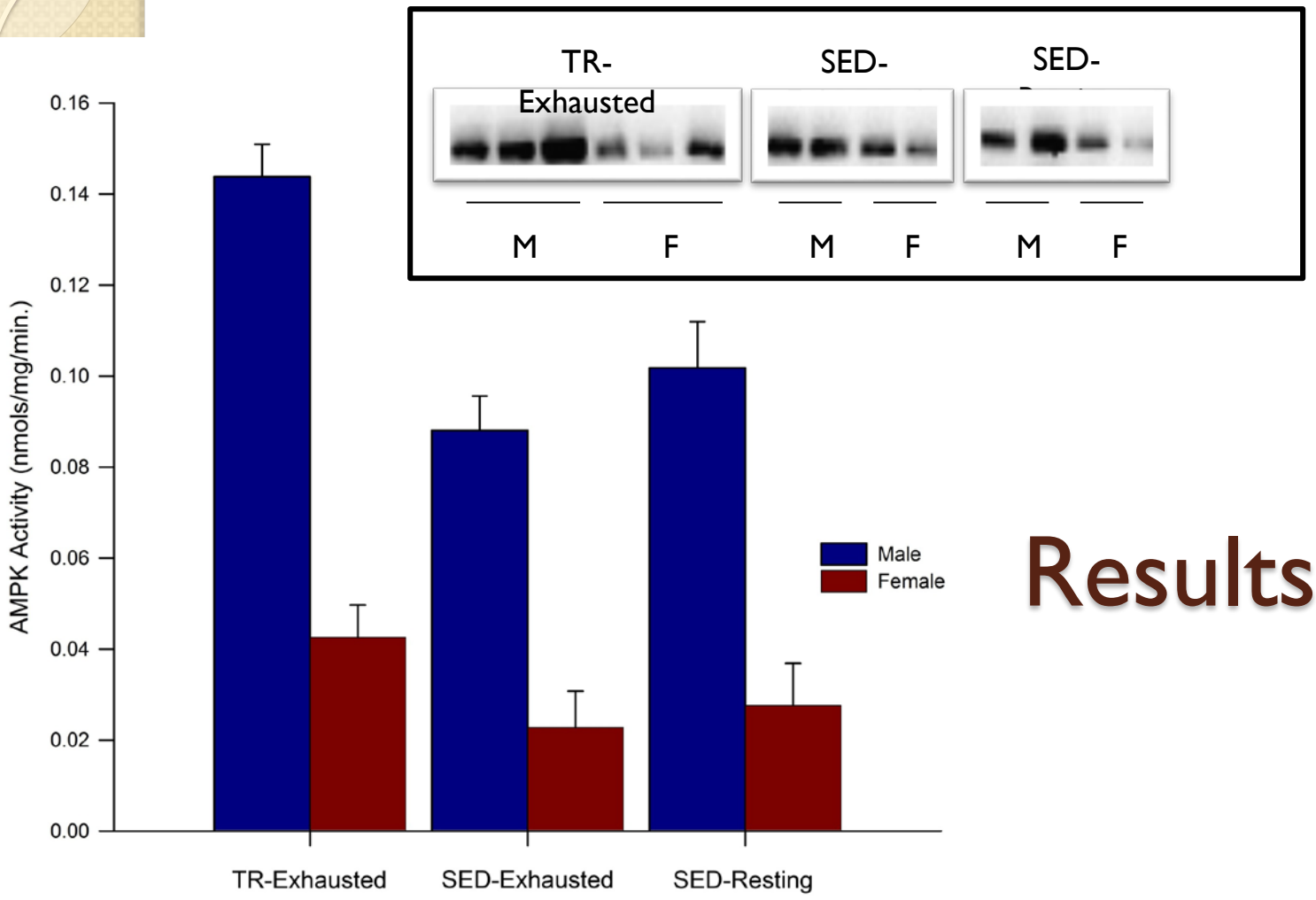
- Subjects:
  - Male (n=25) and female (n=25) C57BL6 mice
  - 13-16 weeks old

- Groups:
  - Sedentary-resting controls
    - males n=5; females n=5
    - no exercise training
    - sacrificed at rest.
  - Sedentary-exhausted animals
    - males n=10; females n=10
    - no exercise training
    - sacrificed after a maximal bout of exercise
  - Trained-exhausted
    - males n=10; females n=10
    - 12-week training period
    - Sacrificed after a maximal bout of exercise

Training Protocol

Table 1: Training protocol; *After day 41 speed and duration are expected to be sustained

Day	Speed (m/sec.)	Time (min.)	Incline	Day	Speed (m/sec.)	Time (min.)	Incline	Day	Speed (m/sec.)	Time (min.)	Incline
0	8	15	25°	**14**	14	35	25°	**28**	22	50	25°
1	8	15	25°	**15**	14	35	25°	**29**	22	50	25°
2	8	15	25°	**16**	16	35	25°	**30**	22	55	25°
3	10	20	25°	**17**	16	40	25°	**31**	22	55	25°
4	10	20	25°	**18**	16	40	25°	**32**	22	55	25°
5	REST	REST	REST	**19**	REST	REST	REST	**33**	REST	REST	REST
6	10	20	25°	**20**	18	40	25°	**34**	22	55	25°
7	10	25	25°	**21**	18	45	25°	**35**	22	55	25°
8	12	25	25°	**22**	18	45	25°	**36**	22	60	25°
9	14	25	25°	**23**	20	45	25°	**37**	22	60	25°
10	12	30	25°	**24**	20	50	25°	**38**	22	60	25°
11	12	30	25°	**25**	20	50	25°	**39**	22	60	25°
12	REST	REST	REST	**26**	REST	REST	REST	**40**	REST	REST	REST
13	14	30	25°	**27**	22	50	25	***41-88**	22	60	25



Results

Fig 3. Left ventricular AMPK activity in trained-exhausted (TR-Exhausted), sedentary-exhausted (SED-Exhausted), and sedentary-resting (SED-Resting) groups for both male and female mice. Values are means ± SEM; n = 10 (Male TR-Exhausted), n = 10 (Female TR-Exhausted), n = 9 (Male SED-Exhausted), n = 8 (Female SED-Exhausted), n = 5 (Male SED-Resting), n = 6 (Female SED-Resting). *P < 0.01 Males vs. Females. †P < 0.01 TR-Exhausted vs. SED-Exhausted and TR-Exhausted vs. SED-Resting.

Discussion

- Humans exercise-induced activation of AMPK in skeletal muscle
  - Males>Females (6)
- Our study suggests a similar relationship in the heart

Discussion: Further Questions

- Male compensatory mechanism?
- Exercise induced AMPK activation=AMPK activation during ischemia?
- How much AMPK activation is needed?
- Why do males still have a larger infarct size?
  - Ceiling effect?
  - Perhaps K_{ATP} channels opening > AMPK activation?

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