What dose of exercise reduces insulin resistance in children, and application to NAFLD

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PLAY PROJECT: HOW MUCH DOES IT TAKE TO REDUCE RISK?

- Tested 2 doses of a daily after-school exercise program on diabetes risk (insulin resistance) in overweight, inactive children

  58% black 42% male
  85% obese 28% prediabetic

- 0 vs. 20 vs. 40 min/day vigorous 3 mo. after-school aerobic exercise program
Baseline Testing

Random Assignment

CONTROL: Monthly family lifestyle class only

LOW DOSE: LC + 20 min/d exercise program

HIGH DOSE: LC + 40 min/d exercise program

EQUAL INTENSITY, GREATER VOLUME

Post-Testing after 3+ months of intervention
Oral glucose tolerance test

Insulin Area Under the Curve (AUC): insulin resistance
Visceral adipose tissue

Subcutaneous fat (green)

Visceral fat (red)
AFTER-SCHOOL EXERCISE PROGRAM

- 8 months (5 days/week)
- Vigorous aerobic activities
  - Fun, simple games – this was not PE
  - running games, jump rope, ball games
- Reward effort, not performance
  - Points for average HR>140 bpm
  - Small weekly prizes
- Transportation provided
• Overweight and obese children
• Fun, simple games – this was not PE
• Reward effort (heart rate) rather than performance (speed, skill)
• Convenient, no cost
20 MIN IS ENOUGH! Vigorous exercise per day to reduce diabetes risk, improve fitness

**Fasting insulin**

**Baseline**

**Posttest**

µU/mL

* p<.05 vs control

Davis et al. *JAMA.* 2012;308(11):1103-1112
VO2 peak

Baseline

Posttest

mL/kg/min

24

26

28

30

32

34

Control

Low-dose

High-dose

P-trend = .02

* p<.05 vs control

Davis et al. *JAMA.*
2012;308(11):1103-1112

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Davis et al. *JAMA.*
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Insulin AUC

Baseline vs Posttest

$P$-trend = .01

* $p < .05$ vs control

* * $p < .01$ vs control

$10^3 \mu U/mL$
** p<.01 vs control

Davis et al. *JAMA*. 2012;308(11):1103-1112
Percent body fat

Baseline

Posttest

36
37
38
39
40
41
42

P-trend < .001

MORE IS BETTER to reduce fatness

Davis et al. *JAMA.* 2012;308(11):1103-1112

* p<.05  *** p<.001 vs control
Davis et al. JAMA. 2012;308(11):1103-1112

Visceral fat

Baseline vs Posttest

Control

Low-dose

High-dose

P-trend < .001

* p<.05 *** p<.001 vs control
Subcutaneous fat

Baseline versus Posttest

- Control
- Low-dose
- High-dose

P-trend < .001

*p < .05 vs high-dose

*** p < .001 vs control

Davis et al. *JAMA.* 2012;308(11):1103-1112
BMI z-score

Baseline

Posttest

1.7
1.8
1.9
2.0
2.1
2.2

Control

Low-dose

High-dose

P-trend < .001

* p<.05 vs high-dose

*** p<.001 vs control

Davis et al. *JAMA.*
2012;308(11):1103-1112
PLAY PROJECT IMPLICATIONS

• 20 min/d aerobic activity can reduce diabetes risk. *Could fit into school day*
  – Optimized PE (SPARK)
  – Classroom PA (Mahar 2006, Donnelly 2009, Kibbe 2011)
  – Recess with adult play leaders (Howe, 2012)
  – Power Up for 30! program led by Georgia SHAPE (georgiashape.org)

• 40 min/d will require after-school time
SMART Study questions

• Are these benefits unique to exercise interventions?
• Will this approach work to reduce risk for arteriosclerosis, NAFLD and NASH in overweight children?
• Would effects be greater over a longer period of time (School year vs semester; 8 vs 3 months)?
Exercise Trials with Liver Fat Outcomes in Children

• Mostly uncontrolled pre-post trials
  – Pacifico et al. 2013, Pozzato et al. JPGN 2010, Van der Heijden et al. 2010

• A few small randomized controlled trials in adolescents have mixed results
  – Lee et al. 2012 (45 obese teen boys)
    • aerobic or resistance exercise ↓ liver fat
  – Lee et al. 2013 (44 obese teen girls)
    • aerobic, but not resistance exercise ↓ liver fat

Why were genders analyzed separately?

– J. Davis et al. 2011 (38 overweight Latina teens)
  • no effect of combined aerobic/resistance exercise on liver fat
STUDY OBJECTIVE:
ISOLATE EFFECTS OF EXERCISE

• To compare cognitive effects of after-school exercise training (40 min/day over 8 months) vs a sedentary attention control condition in overweight children.
  • Effect of exercise *per se*
  • Intent-to-treat analyses

• Ancillary study: arterial stiffness (PWV), liver fat (MRI), liver stiffness (Fibroscan), inflammation (ALT, AST, CRP) outcomes
SEDENTARY CONTROL CONDITION

• Attention control
  – Different room in same building
  – Same buses, same snacks
  – Teachers rotated between conditions

• Sedentary recreation
  • Board games
  • Crafts
  • Teacher-led group activities
  • Points for cooperation, proper use of materials, clean up
  • Points calibrated so groups got equal rewards

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175 healthy overweight, sedentary 8-11 yr olds recruited from Augusta, GA schools

- 61% female, 87% Black
- 9.7 ± 0.9 yrs
- BMI ≥ 85th percentile
- 74% obese
- BMI 26 ± 5 kg/m² (96 ± 4 %ile)
- Percent body fat 38 ± 7 %
- Peak VO₂ 30 ± 6 ml/kg/min
- 92% Needs Improvement-Health Risk

• Groups similar at baseline
RESULTS

- 89% study retention rate at posttest \((n = 155)\)

- Exercise group had 59% attendance rate
  - Heart rate average \(161 \pm 7\) beats/min
  - \(6.8 \pm 1.6\) METs
  - 10 refused posttest

- Control group had 64% attendance rate
  - 10 refused posttest
Dixon Method (2-point) Fat-Water MRI
(scaled to Lipoquant for interpretability)

In-Phase (IP) = W + F

\[
\begin{align*}
\text{Fat-signal index} &= \frac{F}{W+F} = \frac{IP}{2IP} \\
\text{Opposed-Phase (OP)} &= W - F
\end{align*}
\]

Images courtesy of Dr. S. Reeder, U. Wisconsin Madison
Liver Stiffness via Transient Elastography

Fibroscan®, Echosens, Paris, France

- Liver stiffness measurement consists in creating an elastic shear wave within the liver, measuring its speed of propagation and calculating the corresponding stiffness expressed in kilopascals (kPa).

To do so, a probe is placed between the rib bones in proximity to the right lobe of the liver. The operator, assisted by a time-motion mode ultrasonic image, locates a 5-cm deep portion of liver parenchyma free of large vascular structures. When the measurement is triggered, the vibrator gives a painless push to the tissue, creating an elastic shear wave.
Transient Elastography
THANK YOU!

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