Building Healthy Academic Communities Summit

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Director, UCI Institute for Clinical and Translational Science
Today’s Goals

1. How exercise and physical activity influence growth and development in children
2. Role of exercise in prevention across the lifespan
3. Role of exercise in people with chronic disease and disability
4. Discussion, discussion, discussion
Making It Happen! School Nutrition Success Stories
www.cdc.gov/healthyyouth/mh

U.S. Department of Agriculture’s Team Nutrition
www.fns.usda.gov/TN

The U.S. Department of Health and Human Services (HHS) recommends that children and adolescents engage in 60 minutes or more of physical activity every day.  

GUIDELINE 4

Implement a comprehensive physical activity program with quality physical education as the cornerstone.

Children and adolescents should participate in 60 minutes or more of physical activity every day. A substantial percentage of students’ physical activity can be provided through a comprehensive, school-based physical activity program that includes these components: physical education, recess, classroom-based physical activity, walking and bicycling to school, and out-of-school-time activities.
Growth and development: one of the most thrilling elements of the human experience
Growth is impaired in children with chronic disease or disability...

...and so is physical activity.
...so can a deeper understanding of the intersecting biological mechanisms of growth and physical activity enhance exercise-as-medicine in these children?
Aspects of Growth Relevant to Exercise

- **Optimal (healthy) Growth**
  - Genetically pre-programmed and epigenetically modified.
  - Depends on environmental inputs (diet, physical activity, love).
  - Physiological events during growth can influence health across the lifespan.
  - Exquisite coordination among many organ systems.
  - Robust (i.e., catch-up growth is possible, but not always complete).

- Time constrained
Aspects of **Exercise** Relevant to **Growth**

Effects are constrained by mode, frequency and duration.

- **Optimal (healthy) Physical Activity**
  - Stimulates genetic and epigenetic growth adaptive mechanisms.
  - Depends on environmental inputs (diet, technology, "fun").
  - Exquisite coordination among many organ systems.

Improper "dose" can lead to adverse effects.

**Overuse syndrome**
- **Injury**
- **Inflammation (asthma attack)**

**Obesity**
- **Sarcopenia**
- **Impaired neuro-cognitive development**
- **Overuse syndrome**
- **Injury**
- **Inflammation (asthma attack)**
Exercise can stimulate the growth of many tissues

- Muscle
- Mitochondria
- Bone
- Neurons
- Blood vessels
Brief exercise alters health-promoting gene and microRNA expression in circulating monocytes


↑ amphiregulin
↑ epiregulin
↓ TNF
↑ mir-29b
Physical activity in children is not merely play. Rather, it is a fundamental factor in the very process of growth and development.
Children: not just miniature adults—Catch-up growth
Children: not just miniature adults—Catch-up growth
Children: not just miniature adults—Catch-up growth
A Simple View of Exercise and Growth Regulation:

- Hypothalamus
- GRF/SS
- Pituitary
- GH
- Liver
- IGF-1
- Tissue Growth

Stress?

Diet?

Gene expression?
Effect of Exercise on Somatic Growth in the Hamster

THE GH→IGF-I AXIS: FAMILY OF MEDIATORS THAT MIGHT LINK GROWTH, EXERCISE, and NUTRITION

PATTERNS OF PHYSICAL ACTIVITY IN A HEALTHY 7 Y.O.

• Test the hypothesis that exercise training interventions in children and adolescents would lead to increases in circulating IGF-I

But what we actually found was quite the opposite...
Prospective 5-Week Training Studies

- NIH and GCRC supported studies--1995-present
- Endurance exercise-type training programs (↑ energy expenditure 12-15%)
- Coordinated with public school summer programs
Methods

• Doubly-labelled water assessment of energy expenditure
IGF-I Training Paradox

• Muscle mass, cardiorespiratory function, and weight increased, but...

• IGF-I was reduced

• GH and IGF-I binding proteins indicated a catabolic adaptation
“Remember when we used to have to fatten the kids up first?”
Indeed, we know....

- Metabolic Syndrome
- Diabetes
- ↑CV
- Depression
- Learning disorders
- Liver disease
- ↑ in native Americans, Hispanics, African-American
CONCLUSIONS AND RELEVANCE:

Overall, there have been no significant changes in obesity prevalence in youth or adults between 2003-2004 and 2011-2012. Obesity prevalence remains high and thus it is important to continue surveillance.
CONCLUSIONS
Incident obesity between the ages of 5 and 14 years was more likely to have occurred at younger ages, primarily among children who had entered kindergarten overweight.
A Tale of Two Cell-Types

Leukemic Cells

Fat Cells
# COMPARE AND CONTRAST: TWO TROUBLING PEDIATRIC DISEASES

<table>
<thead>
<tr>
<th></th>
<th>Leukemia</th>
<th>Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Occurrence</strong></td>
<td>4.1 cases annually per 100,000 children &lt;15 y.o.</td>
<td>16,000 per 100,000 children &lt;15 y.o.</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>If untreated, invariably fatal</td>
<td>If untreated, few fatalities in children; but many comorbidities</td>
</tr>
<tr>
<td><strong>Cause</strong></td>
<td>Haven’t the foggiest.</td>
<td>Not rocket science.</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Up to 80% longterm survival</td>
<td>Unknown and controversial</td>
</tr>
</tbody>
</table>
CONCLUSIONS AND RELEVANCE:

Overall, there have been no significant changes in obesity prevalence in youth or adults between 2003-2004 and 2011-2012. Obesity prevalence remains high and thus it is important to continue surveillance.
CONCLUSIONS
Incident obesity between the ages of 5 and 14 years was more likely to have occurred at younger ages, primarily among children who had entered kindergarten overweight.
CONCLUSIONS: Obesity is prevalent in pediatric ALL survivors and is independent of patient- and treatment-related characteristics. Clinicians need to screen for obesity and its associated health conditions early in survivorship. *Pediatrics* 2014;133:e704–e715
Why is it happening?
Mammals Protect Stored Fat—Hibernation and Migration
Our human ancestors needed to expend much energy just to find sufficient food....
Not anymore!
Welcome to egrocer.ca
the online supermarket that delivers!

You Click. We Deliver.
Review

Impact of Dietary and Exercise Interventions on Weight Change and Metabolic Outcomes in Obese Children and Adolescents

A Systematic Review and Meta-analysis of Randomized Trials

Mandy Ho, MSc, BHs, APD, RN; Sarah P. Garnett, PhD, M Nutr&Diet, BSc, RNutr, APD;
Louise A. Baur, MBBS, BSc, PhD, FRACP; Tracy Burrows, PhD, BHs, AdvAPD;
Laura Stewart, PhD, BSc, BA, RD, RNutr; Melinda Neve, PhD, BND, APD;
Clare Collins, PhD, BSc, Dip Nutr&Diet, Dip Clin Epi, FDAA

JAMA Pediatrics, 2013
Conclusions

• This review provides support for the importance of dietary interventions as an essential component for managing childhood obesity and provides insights into the impact of different exercise modalities on weight loss and metabolic risk reduction.
Conclusions

• Dietary interventions in conjunction with exercise interventions are effective in reducing metabolic risks, particularly HDL-C and fasting insulin levels, in overweight and obese children in the short term.
Conclusions

• Future studies should aim to strengthen the evidence with rigorous design, appropriate sample size, and longer follow-up periods and should explore better strategies to improve compliance and achieve long-term sustainability.
PEDiatric review

Efficacy of exercise for treating overweight in children and adolescents: a systematic review

E Atlantis¹, EH Barnes² and MA Fiatarone Singh³,⁴,⁵

¹School of Exercise and Sport Science, Faculty of Health Sciences, University of Sydney, NSW, Australia; ²National Health and Medical Research Council: Clinical Trials Centre, University of Sydney, Australia; ³Faculty of Medicine and Faculty of Health Sciences, School of Exercise and Sport Science, University of Sydney, NSW, Australia; ⁴Jean Mayer USDA Human Nutrition Center on Aging at Tufts University, Boston, MA, USA and ⁵Hebrew SeniorLife, Boston, MA, USA
This is the first systematic review and meta-analysis restricted to randomized trials of exercise studies in overweight children/adolescents in the English published literature. We found that exercise significantly reduced percent body fat in obese boys and girls aged approximately 12 years...
A serious gap in our understanding of the effectiveness of childhood obesity intervention is methodological rigor.

The effectiveness of an intervention is hampered by poor design quality that does not measure treatment dose, fails to account for nonadherence, and does not include an adequate follow-up period.
The HEALTHY Study

Funded by:
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
HEALTHY Sample

- 42 middle schools
  - 6 @ 7 field centers
  - 21 randomized to intervention
  - 21 to control (data collection only)

- Eligible schools
  - ≥ 50% minority and/or
  - ≥ 50% eligible for free/reduced lunch

- Eligible 6th graders took PE, had no diabetes, provided consent/assent
HEALTHY Primary Objective

To determine if a COORDINATED SCHOOL HEALTH INTERVENTION PROGRAM affecting the school environment and student behaviors was able to reduce risk factors for T2D in students followed from 6th - 8th grades.
HEALTHY Intervention Program
Four Integrated Components

- Nutrition
- Behavior
- Physical Education
- Communication/Social-Marketing
...and why many others before us have failed in school-based studies...
A School-Based Intervention for Diabetes Risk Reduction

The HEALTHY Study Group*

RESULTS

• The intervention schools had greater reductions in the secondary outcomes of BMI z score, percentage of students with waist circumference at or above the 90th percentile, fasting insulin levels (P=0.04 for all comparisons), and prevalence of obesity (P=0.05).

• Similar findings were observed among students who were at or above the 85th percentile for BMI at baseline.
“So she was considering in her own mind [...], whether the pleasure of making a daisy-chain would be worth the trouble of getting up and picking the daisies...” Alice in “Alice’s Adventures in Wonderland,” Carroll, (1865, p. 11)
Mean cumulative VeSBA (ΔS, g) of successful (solid lines) and unsuccessful (dashed lines) cheetah hunts against time (n = 35, 30 Hz) for (a) steenbok hunts for cheetah individuals A–E and (b) different prey species chased.

Fitness & Cortical Thickness

<table>
<thead>
<tr>
<th>Average Cortical Thickness</th>
<th>Lower Fit (SD)</th>
<th>Higher Fit (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior Frontal</td>
<td>3.55 (0.38)</td>
<td>3.38 (0.43)</td>
</tr>
<tr>
<td>Middle Frontal</td>
<td>3.41 (0.12)</td>
<td>3.35 (0.15)</td>
</tr>
<tr>
<td>Superior Frontal</td>
<td>3.85 (0.14)*</td>
<td>3.76 (0.15)*</td>
</tr>
<tr>
<td>Superior Parietal</td>
<td>2.93 (0.15)</td>
<td>2.89 (0.16)</td>
</tr>
<tr>
<td>Inferior Parietal</td>
<td>3.11 (0.18)</td>
<td>3.07 (0.18)</td>
</tr>
<tr>
<td>Superior Temporal</td>
<td>3.31 (0.19)*</td>
<td>3.17 (0.24)*</td>
</tr>
<tr>
<td>Middle Temporal</td>
<td>3.45 (0.16)</td>
<td>3.41 (0.16)</td>
</tr>
<tr>
<td>Inferior Temporal</td>
<td>3.28 (0.14)</td>
<td>3.21 (0.16)</td>
</tr>
<tr>
<td>Lateral Occipital</td>
<td>2.56 (0.19)*</td>
<td>2.46 (0.10)*</td>
</tr>
</tbody>
</table>
Aerobic Fitness & White Matter Structure

<table>
<thead>
<tr>
<th></th>
<th>Lower fit (M, SD)</th>
<th>Higher fit (M, SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FA corpus callosum genu</td>
<td>0.5277 (0.04)</td>
<td>0.5600 (0.08)</td>
</tr>
<tr>
<td>FA corpus callosum body</td>
<td>0.4125 (0.03)*</td>
<td>0.4510 (0.05)*</td>
</tr>
<tr>
<td>FA corpus callosum splenium</td>
<td>0.5644 (0.02)</td>
<td>0.5789 (0.02)</td>
</tr>
<tr>
<td>FA anterior corona radiata</td>
<td>0.3627 (0.03)</td>
<td>0.3763 (0.07)</td>
</tr>
<tr>
<td>FA superior corona radiata</td>
<td>0.3441 (0.02)*</td>
<td>0.3749 (0.04)*</td>
</tr>
<tr>
<td>FA posterior corona radiata</td>
<td>0.3149 (0.02)</td>
<td>0.3292 (0.02)</td>
</tr>
<tr>
<td>FA superior longitudinal fasciculus</td>
<td>0.3135 (0.01)*</td>
<td>0.3301 (0.02)*</td>
</tr>
<tr>
<td>FA posterior thalamic radiation</td>
<td>0.3971 (0.02)</td>
<td>0.4076 (0.03)</td>
</tr>
<tr>
<td>FA cerebral peduncle</td>
<td>0.4792 (0.07)</td>
<td>0.4684 (0.04)</td>
</tr>
<tr>
<td>RD corpus callosum body</td>
<td>1.000 (0.70)</td>
<td>0.900 (0.16)</td>
</tr>
<tr>
<td>RD superior corona radiata</td>
<td>0.854 (0.05)*</td>
<td>0.781 (0.10)*</td>
</tr>
<tr>
<td>RD superior longitudinal fasciculus</td>
<td>0.928 (0.04)*</td>
<td>0.871 (0.07)*</td>
</tr>
<tr>
<td>AD Corpus callosum body</td>
<td>1.914 (0.12)</td>
<td>1.87967 (0.18)</td>
</tr>
<tr>
<td>AD superior corona radiata</td>
<td>1.486 (0.08)</td>
<td>1.425 (0.11)</td>
</tr>
<tr>
<td>AD superior longitudinal fasciculus</td>
<td>1.459 (0.06)</td>
<td>1.413 (0.09)</td>
</tr>
</tbody>
</table>

RD and AD values are reported in \( \mu \text{m}^2/\text{ms} \). *Significant aerobic fitness group difference, \( p < 0.05 \).
Fitness & Basal Ganglia Volume

Chaddock et al. (2010). Developmental Neuroscience.
Fitness & Hippocampus Volume

Chaddock et al. (2010). *Brain Research.*
Schematic of the overlap between aging and obesity in the cerebral palsy (CP) phenotype.
Filling the Knowledge Gaps and Threading the Needle
Creating a robust biological basis for the “exercise prescription” in children with chronic disease and disability.

- Duration
- Frequency
- Mode
The Challenges We Face:
Technology for All
I can do it. You can do it!