Obesity in Spinal Cord Injury:
Fat Gone Wild!

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Objectives

- Review etiology & incidence of obesity in SCI
- Discuss link between obesity and metabolic syndrome
- Review management options for Obesity / Metabolic Syndrome in SCI

Acknowledgements

- VA Research Career Development Award
- EPVA Scholar Award
- VA RR&D B3307R
- VA RR&D B3158R
- VA HSR&D
- NIDRR K23 Mentor Clinical Research
- NIDRR Model SCI System Grant H133N000009
- NIDRR H133O000274
- NIH NCRR General Clinical Research Grant
- PVA SCRF Grant

Obesity In SCI

- Obesity is at epidemic proportions in SCI
- Obesity is a 2° Condition of SCI due to:
  - Obligatory Sarcopenia
  - Blunted Anabolism
  - Blunted Sympathetic NS
  - Positive Energy Balance
- Obesity mediates:
  - Insulin Resistance
  - Hypertension
  - Dyslipidemia
  - Thromboembolism
  - Coronary Artery Disease

Energy Balance

Energy Expenditure = Energy Intake

Regulation of Food Intake

- External factors: Emotions, Food characteristics, Lifestyle behaviors, Environmental cues
- Central Signals: NPY, AGRP, dynorphin, Orexin-A, CRH/UCN, CART, NE, 5-HT
- Peripheral signals: Glucose, CCK, GLP-1, Apo-A-IV, Vagal afferents, Insulin, Ghrelin, Leptin, Cortisol
- Peripheral organs: Gastrointestinal tract, Adipose tissue, Adrenal gland

Energy Intake
Resting Energy Requirements

- Liver 29%
- Brain 19%
- Heart 10%
- Kidney 7%
- Skeletal Muscle 18%

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Relationship Between REE & FFM

REE (kcal/day)

Fat-Free Mass (kg)

**Acute Energy Needs after SCI**

- Harris Benedict Equation for Males*
  - English: BMR=66.5 + 6.24 (wt in #) + 12.7 (ht in “) – 7.775 (age in yrs)
  - Metric: BMR = 66.5 + 13.75 (wt in Kg) + 5.003 (ht in cm) – 6.775 (age in yrs)
- Harris Benedict Equation for Females*
  - English: BMR=655.1 + 4.35 (wt in #) + 4.7 (ht in “) – 4.7 (age in yrs)
  - Metric: BMR = 655.1 + 9.563 (wt in Kg) + 1.850 (ht in cm) – 4.676 (age in yrs)

Example: 24 y.o. man, 160#, 6'1" after C4 Complete SCI

- Predicted BMR = 66 + 6.23 (160#) + 12.7 (73) – 6.8 (24) = 1826.7 Kcal/d
- Sedentary Correction (1.2): 1826.7 x 1.2 = 2192 Kcal/d
- Stress Correction (1.6): 1826.7 x 1.6 = 2922.7 Kcal/d

Actual REE = 1280 Kcal (43.8% Predicted TDEE)

Represents 1642.7 Kcal/d Positive Energy Balance

11498.9 Kcal/wk (3.2# Fat accumulation/wk)

49281 Kcal/month (14.1# Fat accumulation/month)


**Acute Obligatory N₂ Loss**

- Rodriguez et al, 1991
  - Provided SCI vs Non-SCI
    - 120% Predicted EE (Calories)
    - 2.4 g Protein/kg BMI
  - Continued N₂ loss in SCI until Wk 8
  - N₂ Balance achieved in Non-SCI by Wk 3
- Rodriguez et al, 1997
  - Inappropriate to use PEE, especially not:
    - 1.2 Multiplier (Activity Factor for Bedrest)
    - 1.6 Multiplier (Injury Factor for Major Trauma)

Obligatory Sarcopenia
- Muscle atrophy due to Paralysis
- REE diminishes with N₂ loss


**Definitions**

- **Body Mass Index (BMI)**
  - A measure of a person’s weight relative to his/her height
  - Weight (kg) / Height (m)²
  - Weight (lb) / Height (in)² x 703

Using BMI for Obesity determination

- Underweight BMI < 18.5
- Normal BMI 18.5-24.9
- Overweight BMI 25-29.9
- Obese BMI 30-34.9
- Very Obese BMI 35-39.9
- Morbidly Obese BMI > 40.0

http://www.nhlbisupport.com/bmi/

- **Obesity**
  - High body fat relative to lean body mass (>22% Body Fat)
  - BMI ≥ 30
  - Waist Circumference
    - Men > 42 in (102 cm)
    - Women > 35 in (88 cm)
  - Waist to Hip Ratio (WHR)
    - Waist Circ. / Hip Circ.
    - Men < 0.9 Safe; > 1 @ Risk
    - Women < 0.8 Safe; > 1 @ Risk

http://www.nhlbi.nih.gov/guidelines/obesity/obesity.htm
BMI Underestimates Obesity in SCI

  - Complete Para TDEE 2072 Kcal/d
  - Non-paraplegia TDEE 2582 Kcal/d
- Jones et al, APMBR, 2003
  - LBM ↓ 8.9 kg in SCI
  - Fat ↑ 7.1 kg > in SCI
- Bauman et al, JRRD, 2004
  - Total Body Potassium 2,334 in SCI
  - 3,515 in MZ Twin
  - Resting Energy Expenditure
    - 1,682 Kcal/d in SCI
    - 1,854 Kcal/d in MZ Twin

Body Mass Index in UM SCI Population

Optimal Body Weight?

- Height/weight tables
- Body Mass Index (BMI)
  - Body Weight (Kg) / Height (m²)
- Body composition assessment
- Laboratory techniques
- Field techniques, e.g. skinfold fat

Body Composition Assessment

Cadaver Analyses

- Body Density
  - Fat = 0.901 g/cc
  - FFB = 1.100 g/cc
    - Water = 0.9937 g/cc (73.8%)
    - Protein = 1.340 g/cc (19.4%)
    - Mineral = 3.038 g/cc (6.8%)
- Based on:
  - 3 Male Cadavers
  - Ages 25, 35, 46 y.o.
  - Brozek et al, 1963

Compartment Modeling

- Classic 2-Compartment
  - Cadaver Analysis
  - Fat Mass
- 3-Compartment Model
  - Fat Mass
  - Fat Free Body
  - Total Body Water
  - Fat-Free Dry Mass
- 4-Compartment Model
  - Fat Mass
  - Fat Free Body
  - Total Body Water
  - Bone
  - Residual Dry Mass

Body Composition in SCI

- 4-Compartment Modeling
  - "Gold Standard" (Heymsfeld et al, 1990)
  - Employs 3 Techniques
    - Hydrodensitometry
    - DEXA
    - Deuterium (D2O) Dilution or BIA
  - Compartments include:
    - Fat
    - Total Body Water
    - Bone
    - Residual Dry Mass
Preliminary Findings

### Body Composition Error in SCI

<table>
<thead>
<tr>
<th>Method</th>
<th>Mean ± SE</th>
<th>Range</th>
<th>r</th>
<th>Total Error</th>
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<tr>
<td>4 Comp %Fat</td>
<td>29.3 ± 2.6</td>
<td>7.0 - 62.6</td>
<td>-</td>
<td>-</td>
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<tr>
<td>DXA %Fat</td>
<td>30.3 ± 2.2</td>
<td>10.0 - 63.1</td>
<td>0.73*</td>
<td>7.1 %</td>
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<tr>
<td>UWW %Fat</td>
<td>28.3 ± 2.5</td>
<td>4.8 - 57.0</td>
<td>0.81*</td>
<td>6.0 %</td>
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<tr>
<td>BIA %Fat</td>
<td>23.5 ± 1.9*</td>
<td>8.4 - 57.1</td>
<td>0.57*</td>
<td>11.1 %</td>
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<tr>
<td>J&amp;P %Fat</td>
<td>13.2 ± 1.5*</td>
<td>0.3 - 35.3</td>
<td>0.53*</td>
<td>18.7 %</td>
</tr>
</tbody>
</table>

*p<0.01 vs 4 Comp %Fat


Body Composition in SCI

- Body Fat
- Increased vs. Able-Bodied
- Distribution Differences?
- Fat-Free Body Mass
- JFBB vs. Able-Bodied
- Cardus & McTaggart, 1985
- Spungen et al, 1992
- Bone Density
- Biering-Sorensen et al, 1988
- Finsen et al, 1992
- Total Body Water
- Raasmann Hulnikak et al, 1988

SCI vs. Able Body % Fat

<table>
<thead>
<tr>
<th>Authors</th>
<th>Number</th>
<th>SCI</th>
<th>AB</th>
<th>Gender</th>
<th>Age (Yrs)</th>
<th>BMI (kg/m²)</th>
<th>SCI %BF</th>
<th>AB %BF</th>
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<td>George et al, 1988</td>
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<td>Sedentary M/F</td>
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<td>Para/Tetra</td>
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<td>Active F</td>
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<td>67</td>
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<td>34.2</td>
<td>24.2</td>
<td>DXA</td>
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SCI=Spinal Cord Injury, Para=Paraplegia, Tetra=Tetraplegia, M=Male, F=Female, AB=Able Body Controls, %BF=Per cent Body Fat, D2O=Deuterium Dilution, 4-C Model=Four-Compartment Model, DXA=Dual-energy X-ray Absorptiometry, NA=Not Applicable


Daily Energy Expenditure

- Resting Metabolic Rate
- Thermic Effect of Meal
- Thermic Effect of Activity

UE vs. LE Activity

- LE Work=74-80%LE Work

Energy Metabolism in SCI

- Clark et al, 1966
  - Para (T4-T12; n=7)
  - EE 2209, EI 2193
  - Net 16 Kcal/day
- Mullinger et al, 1986
  - High Tetra (n=14)
  - EE 3332±113, EI 2298±89
  - Net 1071 Kcal/day
  - Net 1071 Kcal/day
  - High Para (n=16)
  - EE 2611±280, EI 2384±740
  - Net -227 Kcal/day
  - Net -227 Kcal/day
- Low Para (n=5)
  - EE 2693±427, EI 2732±866
  - Net 39 Kcal/day
Total Energy Expenditure

2800 Kcal/day

2240 Kcal/day

Physical Activity

Resting Metabolism

Able Body

SCI

Positive Energy Balance

Energy Expenditure < Energy Intake

Net gain: 73,000 Kcal/year = 21 lbs Fat/year

Energy Balance

EE=2340 Kcal/day

EI=2340 Kcal/day

Energy Expenditure = Energy Intake

Obesity Trends* Among U.S. Adults

BRFSS, 2006

(*BMI ≥ 30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC

Obesity Trends* Among U.S. Adults with SCI

Weaver et al, 2007
- 33% Veterans OW
- 20% Frankly Obese
- 22% HTN

Spungen et al, 2003
- Tetra (n=66) 36.3% BF
- Para (n=67) 34.2% BF

Clasey & Gater, 2006
- Para (n=13) 27.2% BF

Obesity / Overfat in SCI

Body Mass Index in VAMC SCI Population
Recent Estimates

- Gupta et al, 2006
  - Site: Milwaukee VAMC
  - N=408, Mean Age 55.8
  - Body Mass Index
    - Underweight 3.6%
    - Normal Weight 27.9%
    - Overweight 35.9%
    - Obese 30.0%
  - Paraplegia > Tetraplegia
  - Reflects FFM in Para + Body Fat Mass

Dangers of Obesity

- Hypertension
- Dyslipidemia
- Type 2 (non-insulin dependent) diabetes
- Insulin resistance, glucose intolerance
- Hyperinsulinemia
- Coronary heart disease
- Angina pectoris
- Congestive heart failure
- Stroke
- Gallstones

Metabolic Syndrome

- Central Obesity
- Insulin Resistance
- Hypertension
- Dyslipidemia
  - High Triglycerides
  - Low HDL-cholesterol

Etiology

- Visceral Obesity is central:
- Adipose secretions
  - Plasminogen Activator Inhibitor (PAI-1)
  - Impaired Fibrinolysis
  - Cytokines (IL-6, TNF-α): Chronic Low-grade Inflammation
  - Angiotensinogen: Vasoconstriction
  - Portal Non-esterified fatty acids (NEFA) ↑ Flux to liver
  - ↑ Triglycerides
  - ↓ HDL-c
- Insulin Resistance due to liver & muscle FFA
  - Hyperglycemia
  - Hyperinsulinemia
  - Hyperlipidemia

Metabolic Syndrome Etiology

- Leptin
  - ↓ Appetite, ↑ BMR
  - Obesity + sensitivity to Leptin

Adiponectin

- CNS
  - ↑ Glucose Disposal
  - ↑ Energy Oxidation
  - ↑ Peripherality
  - Facilitates Insulin Sensitivity
- Resistin
  - From macrophages, not fat
  - ↑ Insulin Resistance
  - Ghrelin (secreted from Stomach)
  - Stimulates hunger (VMN)
  - Stimulates GH release
  - Impairs lipolysis
Adipocytes Impair Fibrinolysis

- Fibrinolysis (Clot breakdown)
- Prevents thrombus formation
- Adipocytes Secrete:
  - Thrombin-Activatable Fibrinolysis Inhibitor (TAFI)
  - Plasminogen Activator Inhibitor-1 (PAI-1)
- TAFI & PAI-1 impair fibrinolysis
- ↑ Risk of Thromboemboli

Diabetes Care 28:2211-2216, 2005

Proinflammatory Adipocytes

- Adipocytes secrete:
  - Interleukin-6 (IL-6)
  - Tumor Necrosis Factor-α (TNF-α)
  - C-Reactive Protein (CRP)
  - ↑ Nuclear Factor Kappa B (NFκB)
  - ↓ Nitrous Oxide
  - Vasodilation
  - Leukocyte Adhesion
  - Endothelial Cell Apoptosis

Diabetes Care 27:2033-2040, 2004
Diabetes Care 27:2960-2965, 2004

Vascular Inflammation in SCI

- Mannis et al, 2005
  - Abdominal sagittal diameter associated with CRP in SCI
- Frost et al, 2005
  - ↑ CRP in SCI vs. AB Controls
- Lee et al, 2005
  - hscRP elevated in SCI
  - hscRP significantly higher in those with metabolic syndrome

Adipocytes cause HTN

- Adipocytes Secrete:
  - Angiotensinogen
  - Platelet Vasoinhibitor
  - Renin-Angiotensin-Aldosterone Syndrome
  - IL-6 → CRP → ↓ NO
  - Diminished Vasodilatation
  - Free-Fatty Acids (FFA)
  - Atherogenesis
  - Poor Compliance arteriola
  - Unusual HTN in SCI

Weaver et al, JSCIM 2007
N=7,959 vets w/ SCI&D
39% BP 120/79-139/89
23% BP >140/90
25% Paral
16% Tetra

Visceral Fat & NEFA

- Visceral Fat
  - Non-esterified Fatty Acids (NEFA)
  - Accumulate in Portal Circulation
  - Liver becomes overwhelmed
    - LDL-c & VLDL-c increases
    - HDL-c diminishes

Dyslipidemia in SCI

- Bauman et al, 1992
  - T-Chol
    - Tetraplegics: 188
    - Paraplegics: 191
    - AB Controls: 210
  - HDL
    - Tetraplegics: 41 ± 1
    - Paraplegics: 37 ± 1
    - AB Controls: 48 ± 2
- Zlotolow et al, 1992
  - Serum HDL in SCI veterans was 35 ± 2 vs. 49 ± 2 in age-matched AB Controls
- Tharion et al, 1998
  - 50% SCI individuals with ↓ HDL; Only 2% with ↑ T-Chol
- Bauman & Spungen, TSCIR 2007
  - 60% SCI had HDL < 40 mg%
  - 44% SCI had HDL < 35 mg%
  - 19% SCI had HDL < 30 mg%

Adipocytes cause Insulin Resistance

- Adipocytes secrete:
  - IL-6
  - TNF-α
  - Resulting CRP highly associated with insulin resistance
  - Accumulation of FFA @ liver and skeletal muscle impair insulin sensitivity
  - FFA diminish glucose concentration gradient
  - PI-3 Kinase Cascade Inhibition
  - Fatty acyl-CoA
  - Diacylglycerol
  - Ceramides

Glucose Transporters

- Hyperinsulinemia & IGT
  - Bauman & Spungen, 1994
    - 34% SCI Impaired Glucose Tolerance (IGT)
    - Additional 22% SCI Frank DM
  - Bauman et al, 1999
    - Impaired Glucose Tolerance
      - 73% Tetra Complete
      - 44% Tetra Incomplete
      - 24% Para Complete
      - 31% Para Incomplete
  - LaVela et al, 2006
    - 20% SCI&D veterans reported DM diagnosis (self-report)

Non-Esterified FAs Inhibit Insulin-Signaling Cascade

- Preliminary Data
  - Glucose during OGTT in SCI
    - * indicates between group differences, p<0.05
    - # indicates between group differences, p<0.05
Preliminary Data

Glucose:Insulin during OGTT in SCI

- All SCI
- C7-T5
- T6-L2
- Normal

* indicates between group differences, p<0.05

T0 T30 T60 T90 T120 T150 T180

Time (Minutes)

C7-L2 (All) SCI Glucose AUC vs. % Body Fat

(4-Compartment Model)

r=0.871, p<0.001

0 10 20 30 40 50 60 70

% Body Fat

0 500 1000 1500 2000

Glucose AUC


T6-L2 Paraplegia Glucose AUC vs. % Body Fat

(4-Compartment Model)

r=0.86, p<0.001

0 10 20 30 40 50 60 70

% Body Fat

0 500 1000 1500 2000

Glucose AUC


Metabolic Syndrome

<table>
<thead>
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<th>Definitions</th>
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<tbody>
<tr>
<td><strong>Central Obesity (Waist Circumference)</strong></td>
</tr>
<tr>
<td>European Men ≥94 cm (37&quot;) or US Men ≥102 cm (40&quot;)</td>
</tr>
<tr>
<td>European Women ≥80 cm (31.5&quot;) or US Women ≥88 cm (34.5&quot;)</td>
</tr>
<tr>
<td>Plus any two of the following:</td>
</tr>
<tr>
<td>- TG ≥150 mg/dl (1.7 mmol/L) or under Rx</td>
</tr>
<tr>
<td>- Low HDL-cholesterol or under Rx</td>
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<tr>
<td>- Men &lt;40 mg/dl (1.03 mmol/L) or Women &lt;50 mg/dl (1.29 mmol/L)</td>
</tr>
<tr>
<td>- Elevated Blood Pressure or under Rx</td>
</tr>
<tr>
<td>- SBP ≥130 mmHg or DBP ≥85 mm Hg</td>
</tr>
<tr>
<td>- Fasting Plasma Glucose ≥100 mg/dl (5.6 mmol/L)</td>
</tr>
</tbody>
</table>

IDF Consensus Panel, August 2005

Holt (2005) Diabetes, Obesity & Metabolism 75(5):618


Metabolic Syndrome in SCI?

- N=487 vets w/ SCI
- Mean Age: 55.2
- 48.7% Tetra
- 56.5% BMI > 25 kg/m²
- 37% Dyslipidemia or Rx
  - 63.4% HDL-c < 40 mg%
  - 48.7% FBG > 100 mg/dl or Rx
- 56.5% HTN
- 44.8% IDF Metabolic Syndrome

Castillo et al., 2007, JSCIM
**Rx Metabolic Syndrome**

- **Diet and Exercise**
  - Sibutramine: Inhibits Norepinephrine reuptake
  - Orlistat: Inhibits pancreatic lipase
  - Metformin (Biguanide): Hepatic Insulin sensitivity ↓
  - Glitizones (Thiozolidinediones): Muscles GLUT4 & Glycogenesis
  - Antihypertensives
  - Lipid-lowering agents

- **Dietary Guidelines for Americans**
  - **Caloric Requirements in SCI**
    - **Tetraplegia**
      - 15-20 lbs < IBW₈₅
      - Recommended Intake:
        - 22.7 Kcal/kg/d
        - 10.3 Kcal/lb/d
    - **Paraplegia**
      - 10-15 lbs < IBW₈₅
      - Recommended Intake:
        - 27.9 Kcal/kg/d
        - 12.7 Kcal/lb/d
      - If "Obese":
        - Use IBW₈₅
        - [(WT_actual – IBW₈₅) x 0.25] + IBW₈₅

  - **Aerobic Exercise Rx**
    - **Limitations:** Ortho, Medical, Time, and Goals
    - **Mode:** Wt-bear vs. Non-Wt-Bearing
    - **Frequency:** 3-5x/week
    - **Intensity:** 55-90% HR_max
    - **Duration:** 20-60 minutes
    - **Progression:** Initial vs. Maintenance

  - **DGA (2005):** 60 min/day Maintenance
  - **ACSM (2005):** 90 minutes/day Weight Loss

  - **Anaerobic Exercise Rx**
    - **Limitations:** Ortho, Medical, Time, Goals
    - **Mode:** Free Weight vs Machine
      - Isometric
      - Isotonic
      - Isokinetic
    - **Frequency:** 2-4x/wk
    - **Intensity:** >65% 1RM
    - **Repetitions:** 1-10
    - **Sets:** 3-6
    - **Recovery:** 2-3 minutes/set
    - **Periodization**

  - **Summary**
    - **Obesity is underappreciated in SCI**
    - **Central mediator of the Metabolic Syndrome**
    - **Epidemic proportions**
    - **Central Obesity**
    - **Dyslipidemia**
    - **High Triglycerides**
    - **Low HDL-cholesterol**
    - **Hypertension**
    - **Insulin Resistance**
    - **Treatment Options**
      - Behavior Modification
      - Pharmacological