Metabolism & Energy Requirements in people with PKAN

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Introduction

• Purpose: to study the metabolism of people with Pantothenate Kinase Associated Neurodegeneration (PKAN)
• Participants: 16 people with PKAN (10 female, 6 male) age range 7 – 69 years, with varying disease severity

Data Collected

• Body Composition by Bioelectrical Impedance
• Disease Severity
• Diet Habit Survey
• Blood and urine markers
• Energy Expenditure at rest (the minimum energy needed for rest and sleeping, without daily activities and movement) was measured by indirect calorimetry (measurement of respiratory gasses) and compared to:
  • Calculation by mathematical equation (WHO equation)
  • People without PKAN (Dietary Reference Intake data)

Body Composition Results

• Overall, PKAN individuals have a normal weight for their height (a normal body mass index, BMI, is 18.5-25)
• Weight due to fat, and non-fat body are on average in a healthy range

Energy Results

• While at rest, people with PKAN use an average of 8% more energy than control subjects (Graph 1)
• People with PKAN use an average of 7% more energy at rest than predicted by the WHO equation (Table 1)
• The respiratory quotient indicates that people with PKAN are burning a normal mix of carbohydrates, fats and proteins

Lab Results

• Normal serum ferritin and transferrin
• No abnormalities in urine organic acids
• Normal plasma amino acids
• Normal lipid panel
• Increased intermediate of cholesterol synthesis in the urine (mevalonate, 30% above normal)
• Normal plasma fatty acids
• Erythrocyte (Red Blood Cell) fatty acid studies showed:
  • Low DHA (average was 3.7, while above 4 is ideal), consistent with a high omega 6, low omega 3 ratio
  • Total polyunsaturated fatty acids 6% above normal

Diet Results & Recommendations

• Compared with the average North American diet of 37% fat, PKAN participants ate a healthier 30% fat diet
• Like the general public, people with PKAN should increase intake of omega 3 (alpha-linolenic) fatty acids
• best source: fish two times per week; fish oil supplements
• Persons with PKAN need approximately 8% more calories per day than people without PKAN

Table 1: Participant Body Composition, Disease Severity, Diet and Energy needs

<table>
<thead>
<tr>
<th>By category:</th>
<th>PKAN Participants</th>
<th>All (n=16)</th>
<th>Ages 19 &amp; up (n=10)</th>
<th>Ages 18 &amp; Under (n=6)</th>
<th>Females (n=10)</th>
<th>Males (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td>25 ± 15</td>
<td>31 ± 15</td>
<td>14 ± 4</td>
<td>25 ± 18</td>
<td>24 ± 10</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td></td>
<td>57.9 ± 18.5</td>
<td>64 ± 17</td>
<td>49 ± 18</td>
<td>52 ± 19</td>
<td>67 ± 15</td>
</tr>
<tr>
<td>Height (cm)</td>
<td></td>
<td>162 ± 16.1</td>
<td>167 ± 12</td>
<td>153 ± 20</td>
<td>157 ± 14</td>
<td>170 ± 14</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td>22 ± 5</td>
<td>23 ± 5</td>
<td>20 ± 4</td>
<td>21 ± 6</td>
<td>23 ± 2</td>
</tr>
<tr>
<td>Body fat percent (% of weight)</td>
<td></td>
<td>21.4 ± 10.0</td>
<td>22 ± 11</td>
<td>21 ± 9</td>
<td>23 ± 11</td>
<td>19 ± 8</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td></td>
<td>13.2 ± 8.90</td>
<td>15 ± 10</td>
<td>10 ± 6</td>
<td>13 ± 11</td>
<td>13 ± 4</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td></td>
<td>45.3 ± 15.2</td>
<td>50 ± 14</td>
<td>36 ± 14</td>
<td>38 ± 10</td>
<td>58 ± 14</td>
</tr>
<tr>
<td>Respiratory quotient</td>
<td></td>
<td>0.90 ± 0.04</td>
<td>0.89 ± 0.04</td>
<td>0.91 ± 0.04</td>
<td>0.89 ± 0.03</td>
<td>0.91 ± 0.05</td>
</tr>
</tbody>
</table>

Severity scales (range):

• Global rating (1-5) 3.4 ± 1.5 3.3 ± 1.5 3.5 ± 1.5 3.6 ± 1.5 3.0 ± 1.4
• Barry Albright Dystonia scale (0-32) 19 ± 7 17 ± 6.6 21 ± 7.5 21 ± 6.7 15 ± 6.4

Diet:

• Diet Habit Survey score (147-389) 160 ± 20 164 ± 23 153 ± 13 158 ± 21 163 ± 20
• Estimated percent fat consumption 30% 30% 30% 30% 30%
• Dietician estimated kcals consumed/day 2150 ± 510 2360 ± 340 1820 ± 600 1990 ± 540 2430 ± 340

Resting Energy Expenditure:

WHO Equation predicted REE (kcal/day) 1450 ± 300 1490 ± 296 1386 ± 323 1280 ± 193 1740 ± 205
IC measured REE (kcal/day) 1570 ± 510 1610 ± 266 1500 ± 393 1401 ± 209 1810 ± 248
IC REE as percent of predicted REE 93 ± 9 93 ± 9 93 ± 10 92 ± 8 95 ± 11

Abbreviations: BMI – Body Mass Index; REE – Resting Energy Expenditure; WHO – World Health Organization; IC – Indirect Calorimetry

Conclusions

• People with PKAN burn more calories even at rest or while sleeping
• Persons with PKAN need an average of 8% more calories than people without PKAN
• Like the general public, people with PKAN should eat a balanced diet including fish oils
• Future research is needed to understand the reasons for and implications of a high cholesterol precursor (mevalonate)

Acknowledgements

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• Oregon Clinical & Translational Research Institute, TL1

Graph 1: Resting Energy Expenditure (REE, kcal/day) vs. Body Weight (kg) depicts the dots for each person and a line of best fit for the two groups, those with and without PKAN. The slopes of the lines are equal (increasing weight corresponds with increasing REE), and the PKAN REE is notably 8% higher than the control group.