Symptom clusters, stress and cognition in survivors of childhood leukemia and CNS malignancies

Kevin R. Krull, PhD
Department of Epidemiology and Cancer Control
St. Jude Children’s Research Hospital

IOM/NRC BCYF
March 10, 2011
Objectives

- To present patterns of symptoms in long-term survivors of childhood cancer
- To review associations between symptom clusters and cognition
- To discuss biomarkers of stress and cognitive outcomes in survivors of childhood leukemia and CNS malignancies
Symptoms by Treatment Intensity

N= 285 Adult Survivors of ALL
Note: Impairment = <10th %ile on age-adjusted normative scale

(Krull et al, ASCO)
### ADHD Symptoms in ALL Survivors

<table>
<thead>
<tr>
<th>Inattentive</th>
<th>Never</th>
<th>Occasional</th>
<th>Often</th>
<th>Very Often</th>
<th>% Impaired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty organizing tasks</td>
<td>95</td>
<td>33</td>
<td>18</td>
<td>15</td>
<td>20%</td>
</tr>
<tr>
<td>Avoids sustained effort</td>
<td>83</td>
<td>39</td>
<td>24</td>
<td>15</td>
<td>24%</td>
</tr>
<tr>
<td>Easily distracted</td>
<td>64</td>
<td>45</td>
<td>25</td>
<td>26</td>
<td>32%</td>
</tr>
<tr>
<td>Forgetful in daily activities</td>
<td>77</td>
<td>49</td>
<td>19</td>
<td>16</td>
<td>22%</td>
</tr>
</tbody>
</table>

### Hyperactive/Impulsive

<table>
<thead>
<tr>
<th>Hyperactive/Impulsive</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fidgets with hands or feet</td>
<td>59</td>
<td>50</td>
<td>29</td>
<td>23</td>
<td>32%</td>
</tr>
<tr>
<td>Talks excessively</td>
<td>93</td>
<td>34</td>
<td>15</td>
<td>19</td>
<td>21%</td>
</tr>
</tbody>
</table>

### Symptoms Pervasive

<table>
<thead>
<tr>
<th>Symptoms Pervasive</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>67</td>
<td>35</td>
<td>29</td>
<td>30</td>
<td>37%</td>
</tr>
</tbody>
</table>

### Functional Impairment

- No=120
- Yes=41

### Full DSM-IV Criteria

- No=144
- Yes=17

N=161 Child/Adolescent survivors of ALL

(Krull et al, 2011)
Fatigue in Child Cancer Survivors

Fatigue Scores

- General Fatigue
- Sleep/Rest Fatigue
- Cognitive Fatigue

Healthy Survivors

N=102 Healthy Controls, 95 Child Survivors

(Varni et al, 2002)
Quality of Life in Adult Survivors

N=388 siblings, 2,090 ALL, 786 CNS Tumors

(Zeltzer et al, 2008)
Post-Traumatic Stress Disorder

N=6,542 adults survivors of childhood cancer
Adjusted for age, sex, race

(Odds Ratio)

Stuber et al, 2010
### Risk of Chronic Health Conditions

**N=10,397 survivors, 3,034 siblings**

(Oeffinger et al, 2006)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>RR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sibling</td>
<td>1.0</td>
<td>31.2-48.5</td>
</tr>
<tr>
<td>Bone Tumor</td>
<td>38.9</td>
<td>10.3-15.5</td>
</tr>
<tr>
<td>CNS Tumor</td>
<td>12.6</td>
<td>8.3-12.5</td>
</tr>
<tr>
<td>Hodgkin’s</td>
<td>10.2</td>
<td>5.3-8.6</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>6.8</td>
<td>3.5-6.4</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>4.7</td>
<td>3.4-5.1</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4.1</td>
<td>3.2-5.4</td>
</tr>
<tr>
<td>Wilm’s</td>
<td>4.1</td>
<td>3.2-5.4</td>
</tr>
</tbody>
</table>
Symptom Clusters in CNS Tumors

N=810 adult survivors of childhood CNS tumors
Adjusted for age at diagnosis, sex, and CRT dose to other regions

(Armstrong et al, 2010)
Obesity in Adult Survivors

N=1,652 adolescents followed to adulthood (18% obese)
Adjusted for sex, CRT dose, and adolescent obesity

(Krull et al, 2010)
Physical Activity and Cognition

N=6,440 adult survivors of childhood cancer
Adjusted for age, sex, diagnosis and BMI

(Krull et al, in press)
Symptom Interaction

Moderators of Living Independently

- Current Age
- Race
- Age @ Diagnosis
- Cranial Radiation Therapy
- Growth Hormone Deficiency
- Chemotherapy
- Diagnosis

Physical Endurance → Med Use

Task Efficiency → Depression

Somatization → Memory

Mental Health → Emotional Regulation

Mental Health → Vitality

R² = 43%

CFI = 0.997
TLI = 0.998
RMSEA = 0.019
P, RMSEA ≤ .05 = 1.000

N=4,407 survivors ≥ 25 years old

(Kunin-Batson et al, 2011)
Cognition and Steroids

N=40 adult survivors of ALL (Krull et al, ASH)
Serum Cortisol

N=40 adult survivors of ALL

(Krull et al, ASH)
Categories of polymorphisms

- Key enzyme pathways associated chemotherapy (e.g. anti-folate therapy, corticosteroid therapy)
- Oxidative stress or other processes that may affect the biological response to CNS treatments
Folate Pathway: Behavioral risk

N=72 child survivors of ALL (>5 yrs post diagnosis)  (Kamdar et al, in press)
Polymorphisms: Shifting Attention

N = 72 child survivors of ALL (>5 yrs post diagnosis) (Kamdar et al, in press)
Survivors of childhood cancer present with long term cognitive, physical, and emotional late effects. Symptoms across these categories are interactive. Physical and/or emotional stress may exacerbate or maintain symptoms across development. Preventative and therapeutic interventions specific to these cohorts are needed to address long-term risk.