Agenda

- Why is Working Memory Training Salient for Cancer Survivors?
- Cogmed Specific Studies & Cancer
  - 2015, Cox, et al., Childhood cancer survivors.
  - 2015, Conklin, et al., Childhood cancer survivors.
What is Cogmed?
Computerized Cognitive Training targeting Working memory.

DEMO?
• Go to: http://my.cogmed.com/
• Or: my.cogmed.com

• Choose Version:
• Choose Language:

Pediatric Cancer
(Hardy, CNMC, 2012)

❑ 36 children are diagnosed with cancer every day
  □ The average age at diagnosis is 6-years-old, but more are diagnosed under age 5 and over age 12
❑ Aggregated survival rate is about 80%
  □ There are about 350,000 adult survivors of childhood cancer in the US, which equates to 1 in 640 adults
❑ Recent shift in research/clinical emphasis from simply curing cancer to improving quality of life during survivorship

Most common post cancer treatment cognitive problems.
(Hardy, CNMC, 2012)

Decreased attention
Impaired working memory
Slowed processing speed and reaction time
Weak visual-motor skills
Diminished ability to learn and recall
Language functioning is often relatively intact

Skills that develop before treatment aren’t as affected as the part of the brain that develops after treatment
Cognitive Effects of Cancer Treatment:
(Hardy, CNMC, 2012)

- Changes in learning and memory that occur after treatment has ended, usually beginning around a year or more after completion of therapies
- May be noticed first when
  - Children have trouble learning new material
  - Children seem to easily forget what they have learned
  - Children work more slowly than they used to, or have difficulty finishing their work

Over 75 Cogmed published studies, several with healthy adults
(*randomized, placebo controlled, *independent investigators)

Population
- Typical
- ADHD/ Special needs
- Brain Injury/Strokes/MCI
- Cancer
- Hearing Loss
- Developmental Psychiatric Problems
- Low WM or academic Achievement

Adults - Children/ Adolescents - Preschoolers

![Children & Adolescents with Cancer & Cogmed.](image)
(Hardy, Willard, Allen, & Bonner, 2012)

- 20 children aged 8-16 (85% Caucasian) randomized to complete either an adaptive or non-adaptive version of Cognemed
- Children off treatment at least one year and medically stable
- Everyone loaned a laptop to complete training
  - Same coach for all participants
- 85% of children finished the program
  - Rotating data link VERY difficult for a number of participants
- No adverse effects

Working Memory: WRAML2
(Hardy, Willard, Allen, & Bonner, 2012)

Parent Report: CONNERS-3
(Hardy, Willard, Allen, & Bonner, 2012)
Conclusions
(Hardy, Willard, Allen, & Bonner, 2012)

- Cogmed RM is a feasible method of addressing working memory deficits in survivors of pediatric cancer.
- Survivors with better overall cognitive functioning appear to benefit more from the training, though this merits further study.
- Training may not be generalizing to a broad range of cognitive outcomes, at least soon after finishing the program.
- No differences were found in verbal working memory.
  - “Dose” of training may need to be increased.
  - Cancer survivors may be limited in how much they can improve given the nature of their deficits.

(Lauren E. Cox, Jason M. Ashford, Kellie N. Clark, Karen Martin-Elbahesh, Kristina K. Hardy, Thomas E. Merchant, Robert J. Ogg, Sima Jeha, Victoria W. Willard, Lu Huang, and Heather M. Conklin et al., 2015)

- n=68, 34 treatment, 34 control aged 8-16 (85% Caucasian), aver. Age=12.2, at least 1 year post therapy. 32% had brain tumors, 68% had acute lymphoblastic leukemia (ALL).
- Focus upon feasibility and acceptability.
- Participants lived in 16 states. 30 of 34 completed Cogmed (88%).
- Almost all completed pre/post-intervention neuroimaging exams (91% & 93%)
- Remotely administered. Single-blind, randomized, wait-list control design.
- Majority of brain tumor patients, 72.2% were treated with cranial radiation therapy and the 87% of the ALL participants were treated with chemotherapy.
- Patients completed 25 WM sessions over 5-9 weeks at home with weekly phone-based coaching.

Geographical breadth of study.
(Cox, et al., 2015)
(Cox, et al., 2015)

- Families had the necessary skills to use Cogmed successfully. Caregivers reported that they were able to find the time to complete to complete training (63%), viewed training as beneficial (70%) and would recommend this intervention to others (93%).

- Conclusion: Cogmed is feasible and acceptable for childhood cancer survivors. It is viable even for those survivors who do not live in close proximity to cancer care centers. Efficacy and neural correlates of change are being evaluated (and will be published in another study).

"Computerized Cognitive Training for Amelioration of Cognitive Late Effects Among Childhood Cancer Survivors: A Randomized Controlled Trial"

- Results: Survivors completing the intervention (n = 30; 88%) demonstrated greater improvement than controls on measures of working memory (mean ± SEM; eg, Wechsler Intelligence Scale for Children [fourth edition; WISC-IV] spatial span backward, 3.13 ± 0.58 v 6.75 ± 0.43; P = .002; effect size [ES], 0.84).

- Attention (eg, WISC-IV spatial span forward, 3.30 ± 0.71 v 1.25 ± 0.39; P = .01; ES, 0.65).
- Processing speed (eg, Conners' Continuous Performance Test hit reaction time, −2.10 ± 1.47 v 2.54 ± 1.25; P = .01; ES, 0.61).

- Greater reductions in reported executive dysfunction (eg, Conners' Parent Rating Scale III, −6.73 ± 1.51 v 0.41 ± 1.53; P = .002; ES, 0.84).

- Functional magnetic resonance imaging revealed significant pre- to post-training reduction in activation of left lateral prefrontal and bilateral medial frontal areas.

"Computerized Cognitive Training for Amelioration of Cognitive Late Effects Among Childhood Cancer Survivors: A Randomized Controlled Trial" (Conklin, et al., 2015)

- "Children receiving CNS-directed therapy for cancer are at risk for cognitive problems, with few available empirically supported interventions. Cognitive problems indicate neurodevelopmental disruption that may be modifiable with intervention. This study evaluated short-term efficacy of a computerized cognitive training program and neural correlates of cognitive change."

- Same sample as the Cox, et al., 2015 study.
Cognitive Remediation Therapy for Brain Tumor Survivors with Cognitive Deficits
(Sacks, et al., 2015)

n=3, Ages: 63 (M), 27 (F), 53 (M).

Cognitive deficits have been widely observed in patients with primary brain tumors consequent to diagnosis and treatment. Given the early onset and the relatively long survival rate of patients, it seems pertinent to study and refine the techniques used to treat these deficits. The purpose of this article is to discuss cognitive deficits that follow neurosurgical treatment for low-grade gliomas as well as to outline a neuropsychological intervention to treat these deficits, specifically working memory and attention. Cognitive remediation therapy is a neuropsychological intervention that aims to enhance attention, working memory, and executive functioning, thereby diminishing the impact of these deficits on daily functioning. Computerized cognitive remediation training programs facilitate access to treatment through providing online participation.

“The results so far suggest some improvement in working memory and attention from baseline scores. It is the hope of the present authors to highlight the importance of this treatment in the continuity of care of brain tumor survivors.”

1. Attention: Digit Span Forward (WAIS-IV), Rey’s Auditory Verbal Learning Test (RAVLT) Trial 1.
4. Mood: Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI).

Subjects improved scores in all of these domains.
"Cognitive Remediation Therapy for Brain Tumor Survivors with Cognitive Deficits"  
(Sacks, et al., 2015)

"The results obtained so far suggest that Cogmed® may help improve scores in the aforementioned domains.

For digit span forward, participant 1 showed improved scores immediately after completing Cogmed® training, and participants 2 and 3 showed improved performance when tested at the third time point (three-month follow-up).

For digit span backward, participant 1 showed increased scores at both the second and third time points while participants 2 and 3 exhibited improvements in scores at the second time point. For letter-number sequencing, only participant 2 showed some improvement."
All three showed an overall improvement in performance from baseline to follow-up scores.

Mood measured by Beck Depression Inventory (BDI) & Beck Anxiety Inventory (BAI):

"Cognitive Remediation Therapy for Brain Tumor Survivors with Cognitive Deficits"

Conclusion: This preliminary data suggest that Cogmed merit further investigation for "its role in facilitating post-illness functioning for survivors. The present investigators are actively recruiting patients with relatively good prognoses to study the efficacy of Cogmed® in helping restore functioning, assisting with reintegration, and consequently improving the quality of life. CRT is an essential part of the continuity of care for post-treatment neurosurgical patients in order to enhance the quality of life and assist with reintegration into vocational and/or academic environments. Computerized CRT allows access to these interventions and warrants further investigation to establish its efficacy and effectiveness."
Variable Protocol: 25 min, 35 min vs. Standard
Note ages of subjects in this internal review.

Variable Protocol Results Suggest it may be helpful for TBI patients.

Results - training improvements
There were no significant differences in training improvements when comparing the three different protocols (p-values > 0.05). There was however a significant difference in improvement on the training tasks for the different protocols, with the standard protocol being associated with higher index improvements (p < 0.05). These effects are summarized in Table 2 and Figure 1.

<table>
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<th>n</th>
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<td>5.62</td>
<td>7.08</td>
<td>15.36</td>
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</tr>
</tbody>
</table>

Table 1: Summary statistics for training age of subjects across protocols. Average and standard deviations are presented for age, start index, and the three CPT tasks. Standard deviations were calculated for training age, start index, and the three CPT tasks. These values are presented in Table 2. Following instructions, and help up (AU), previously called the Notch Challenge.
Summary

- We reviewed prevalence rates for pediatric cancer, survival rates and estimate the number of children returning to school with cognitive problems.
- We described the cognitive impairments commonly found in survivors: these include working memory, attention, processing speed, reaction time, visual motor skills and ability to learn new material.
- However, these problems may not be immediately evident...we may need to wait for therapies to be complete. And these cognitive problems may emerge gradually, even a year later in some cases.
- In the research by Hardy, there were 20 children who showed improved performance on the symbolic memory on the WRAML and improved scores in learning problems on the Conners.
- In Cox’s study there were 68 participants. 70% of parents saw improvement, 93% would recommend the program to others.
- In the Conklin study improved performance was noted in working memory, (WISC scores for Spatial Span Backwards), in attention (WISC Spatial Span Forward) and in processing speed (Conners) & Executive functions (Conners).
- Also noted were improvements in MRI scans with reduced activation in bilateral frontal areas of the brain.
- And in Sacks feasibility there were suggestions that Cogmed (CRT) could lead to better outcomes in adults too.

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