



Working Memory Training & Cancer



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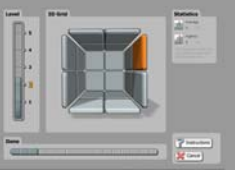


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Agenda

- **Why is Working Memory Training Salient for Cancer Survivors?**
- **Cogmed Specific Studies & Cancer**
 - 2012, Hardy, et al., Pediatric cancer survivors pilot study.
 - 2015, Cox, et al., Childhood cancer survivors.
 - 2015, Conklin et al., Childhood cancer survivors.
 - 2015, Sacks, et al., Adults Tumor Survivors with Cognitive Deficits.




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What is Cogmed?

Computerized Cognitive Training targeting Working memory.
DEMO?

- Go to: <http://my.cogmed.com/>
- Or: my.cogmed.com




•Choose Version:

Select Language

	British English		US English
	French		Norsk (Bokmål)
	Nederlands		Svenska
	Italiano		Português (Brasil)



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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


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

Population	Adults	Children/ Adolescents	Preschoolers	
Typical	Klingberg et al., 2002 (exp. 2) Olesen et al., 2004 Westerberg & Klingberg, 2007 McLach et al., 2009 Brodmier et al., 2009, 2011, 2012 Bellander et al., 2011 *Gibson et al., 2012, 2013 *Dunning & Holmes, 2014 *Karyenborghs, et al., 2016 *Johnson-Buckley, et al., 2016	*Holmes & Gathercole, 2014 (Trial 1) *Kadic, et al., 2015 Soderqvist et al., 2014 *Dunning & Holmes, 2014 *Gibson et al., 2012, 2013, 2014 *Fath, et al., 2015 Soderqvist & Nader, 2015	*Thorell et al., 2009 *Bergman-Nyberg et al., 2011 Soderqvist et al., 2012	
ADHD/ Special needs	Grapper et al., 2014 *Mawson et al., 2014	*Klingberg et al., 2002, 2005 *Holmes et al., 2010 *Gibson et al., 2010 *Mazzucchi et al., 2010 *Buck et al., 2010 *Dahlin, 2010, 2011 *Green et al., 2012 *Gray et al., 2012 *Egeland et al., 2013 *Gibson et al., 2013 *Hovik et al., 2013 *van Bergen-Bosterman et al., 2014 *Stooper, et al., 2015		
Brain Injury/Stroke/MCI	Westerberg et al., 2007 *Lundqvist et al., 2010 *Johnson & Forman, 2011 *Akurand et al., 2013 *Egeland et al., 2013 *Hollgren et al., 2015 *Horneij et al., 2015	*Hardy et al., 2012 *Cox, et al., 2015 *Conklin et al., 2015 *Sacks et al., 2015		
Cancer				
Hearing Loss Developmental Psychiatric Problems	*Saunders et al., 2014 *Ferguson & Hershaw, 2015 *Maroti et al., 2015	*Kronenberg et al., 2010 *Lahaugren et al., 2011 *Roughley & Holmes, 2011 *Bergqvist et al., 2013	*Soderqvist et al., 2012 *Grunewald et al., 2013	
Low WM and/or Academic Achievement		*Holmes et al., 2009 *Holmes & Gathercole, 2014 (Trial 2) *Dunning et al., 2013 *Bergman-Nyberg & Klingberg, 2014 *Holmes et al., 2015 *Kim, et al., 2015		





Children & Adolescents with Cancer & Cogmed.




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Working Memory Training in survivors of pediatric cancer: randomized pilot study.

(Hardy, Willard, Allen, & Bonner, 2012)

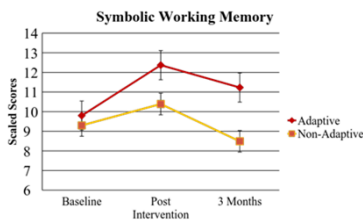
- 20 children aged 8-16 (85% Caucasian) randomized to complete either an adaptive or non-adaptive version of Cogmed
- Children off treatment at least one year and medically stable
- Everyone loaned a laptop to complete training
 - Same coach for all participants
- **85% of children finished the program**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



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Working Memory: WRAML2

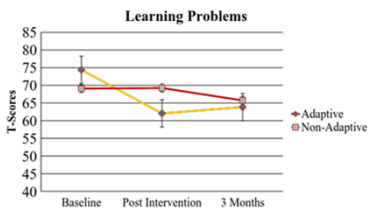
(Hardy, Willard, Allen, & Bonner, 2012)



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Parent Report: CONNERS-3

(Hardy, Willard, Allen, & Bonner, 2012)



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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.



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Working Memory Training in survivors of pediatric cancer: randomized pilot study.

Lauren E. Cox, Jason M. Ashford, Kellie N. Clark, Karen Martin-Elbahesh, Kristina K. Hardy, Thomas E. Merchant, Robert J. Ogo, Sima Jeha, Victoria W. Willard, Lu Huang, Hui Zhang 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.



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Geographical breadth of study.

(Cox, et al., 2015)

Geographical Distribution of Cogmed Training



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Working Memory Training in survivors of pediatric cancer: randomized pilot study.

(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).



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

(Heather M. Conklin, Robert J. Oun, Jason M. Ashford, Matthew A. Scoggins, Ping Zou, Kellie N. Clark, Karen Martin, Elbahesh, Kristina K. Hardy, Thomas E. Merchant, Sima Jeha, Lu Huang and Hui Zhang, 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.

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

(Conklin, et al., 2015)

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 0.75 ± 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 = .02; **ES, .61**) and


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.**”

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Adults with Cancer & Cogmed.




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“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.”


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“Cognitive Remediation Therapy for Brain Tumor Survivors with Cognitive Deficits”
(Sacks, et al., 2015)

“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.
2. **Working memory:** Digit Span Backward (WAIS-IV), Brief Test of Attention-Letters, Letter-Number Sequencing (WAIS-IV).
3. **Memory:** RAVLT Short Delay Free Recall (SDFR) and Long Delay Free Recall (LDFR).
4. **Mood:** Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI).

Subjects improved scores in all of these domains.

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“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.

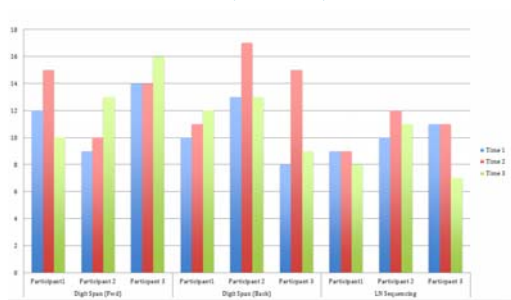
For digit span forward, participant 1 showed improved scores immediately after completing Cogmed® training, and participants 2 and 3 showed improved performance when tested at the third time point (three-month follow-up).

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.”



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WAIS-IV
(Sacks, et al., 2015)

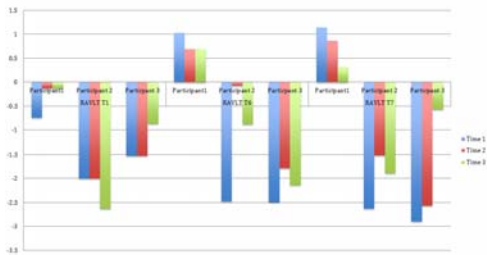


Time 1: Pre-testing
Time 2: Immediately post Cogmed.
Time 3: 3 months post Cogmed

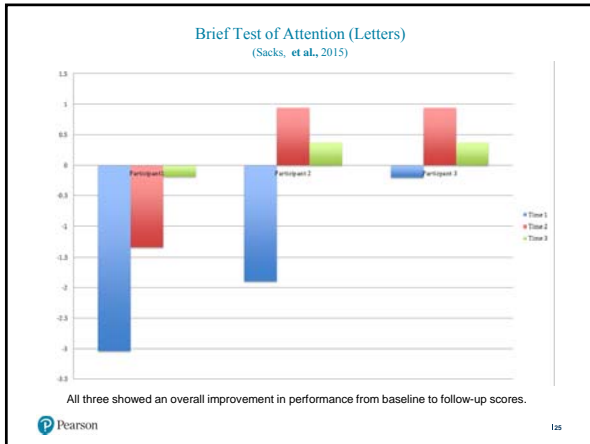


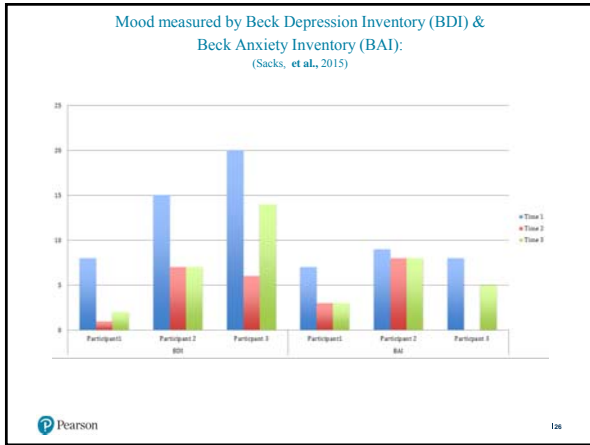
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RAVLT
(Sacks, et al., 2015)



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“Cognitive Remediation Therapy for Brain Tumor Survivors with Cognitive Deficits”

(Sacks, et al., 2015)

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.”

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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' 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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