Will Children with ADHD, Learning Problems and Learning Disorders respond Differently to Cogmed?

September 21, 2016

Agenda

- How does Working Memory, the Target of Cogmed, relate to ADHD, Learning Disabilities & Learning Problems?
- Potential limiting & facilitating factors to far transfer of Cogmed effects.
- Cogmed-specific study with ADHD, LD & Learning Problems.
Cogmed Trains Working Memory.
What is Working Memory (WM)?

A system for temporary storage and manipulation of information, necessary for a wide range of cognitive tasks

- To keep information in your mind for a short period of time (seconds) & use in your thinking
- Processes all stimuli we encounter - updating
- Delegate to different parts of our brain to take action - shifting
- Allows us to block out unnecessary information - inhibition
- Keeps us updated on what’s happening - & focused on what matters

The Lack of Development of Working Memory (WM) in ADHD.
How VSWM became the target for Cogmed.


How does WM of those with ADHD affect learning?
Poorer WM = more errors, slower learning, no automaticity.
(Huang-Pollock & Karalunas, 2010)

When a task has a low WM demand
Children with ADHD still make more errors and learn it more slowly.

When a task has a high WM demand
Children with ADHD don’t get to automaticity.

Result of those struggles: A distinct trajectory of low academic achievement.
Learning disabilities.
(Rutherford-Ragetli, et al., 2016)

“Learning disabilities” refers to “roughly into two groups: specific learning disorders (LD), and general learning problems.”

“LD, like dyslexia or dyscalculia, refer to specific problems in a single domain of learning capacities or academic achievements.”

“Dyslexia is characterized by a specific and significant impairment in the development of reading skills (problems with accurate or fluent word recognition, poor decoding, poor spelling), while dyscalculia is characterized by a specific impairment in the acquisition of mathematical skills (Problems with processing of numerical information, learning arithmetic facts, performing accurate and fluent calculations).”

Consider Deficits associated with Dyslexia:
Poor Phonological Loop & Central Executive
(Dawes, et al., 2015)

“Poor readers” matched by age and gender with typically developing readers.

Measures: Phonological loop, central executive, visuospatial sketchpad & episodic buffer.

Poor readers were worse on phonological loop and Central Executive only.

Plot thickens: Processing speed, temporal processing and WM play a role in SLI.
(Moll, et al., 2016)

N=99, 4 groups, reading disability (RD), math disability (MD), both, Typically developing.

There are high comorbidity rates between RD & MD.

diff 3 risk factors related to poor attention: Processing speed, temporal processing & WM.

Control for attention and RD & MD differed, but both RD & MD had worse verbal memory than typically developing children.

RD worse processing speed but was restricted to nameable symbols.

MD associated with temporal processing and visuospatial memory deficits.
Meta-Analysis of oral language deficits in familial dyslexia
(Snowling & Melby-Lervag, 2016)

Preschoolers: Phonological processing deficits, broader language skills (letter knowledge, phonological awareness & rapid automatized naming (RAN)) deficits.

Longitudinal studies: More severe impairments in preschool language than those defined as normal. Poor phonological awareness & literacy skills. Parents lower educational levels & read less frequently to themselves.

Pennington’s multiple deficits view of dyslexia
(Carroll, et al., 2015)

Deficits in phonological awareness, print knowledge & rapid naming predict later reading difficulties. N=267 children tested with wide battery of tasks associated with dyslexia. Then tested 2, 3, and 4 years later. 42 poor readers were later identified.

Deficits: Yes print knowledge, verbal short-term memory, phonological awareness and rapid naming were good predictors of later poor reading.

Also deficits in visual search and auditory processing present in a large minority of poor readers.

Almost all poor readers showed deficits in at least one area.

No single deficit characterized the majority of poor readers.

HENCE: Supported Pennington’s multiple deficits view of dyslexia. Multiple interacting factors combine to result in poor reading.

Intervening in only WM and/or STM may not address all deficits that have lead to poor reading.

Learning Problems.
(Rording-Ragetlie, et al., 2016)

Difficult to differentiate. Yet has significant clinical relevance.

“The term general learning problems refers to non-specific and possibly co-occurring disabilities in the following areas: 1) receptive language; 2) expressive language; 3) basic reading skills; 4) reading comprehension; 5) written expression; 6) mathematical calculation and reasoning; and 7) attention (Lyon, 1996).”

“The group of learning problems is a heterogeneous group characterized by a broad range of symptoms covering diverse academic achievement problems. Although symptoms may (at some stage) not meet DSM criteria for ADHD or LD, they may be associated with sub-threshold psychiatric problems. Children with learning problems may be “overlooked” struggling students, meeting minimal academic standards, often caused by processing strength and weaknesses that adversely affect school achievement.”

It appears somewhat more likely that WM deficits may be a bottleneck among these students, but this a diverse and poorly defined group making this unclear.
Improved WM has potential to have a notable impact upon learning, but there are limiting or facilitating factors.

Can improving WM open the door to gains? Are there factors which may limit or facilitate gains?

Limiting factors?
- ADHD-C?
- Comorbid disorders?
- Learning Disabilities?
- Learning Problems?

Facilitating factors?
- Dosing of Cogmed?
- Motivation?
- Rx?
- Cogmed-Plus?
- Domain general training?
- Domain specific training?

Cogmed with children with Different Neurodevelopmental Disorders (ADHD, LD, Learning Problems)
(Rording-Ragetlie, et al., 2016)

N=99, ADHD (n=45), LD (n=34), learning problems (n=20). Ages (7-17).
25 sessions of Cogmed.
WM, ADHD DSM-IV rating scales BRIEF scales used to measure outcomes.

Hypothesis: "training effects may lie on a continuum with those of the LD group at the lower end and those of the learning problems group at the upper end."

Results: Partially confirmed the hypothesis in that all groups improved significantly with ADHD children or children with learning problems showing the best results.

http://dx.doi.org/10.4236/psych.2016.73034
ADHD (n=45), n=7 taking Rx (6 stimulants, 1 Methylphenidate). Rx stable before and after Cogmed.

- ADHD-I (n=25), Note: A majority of those with ADHD has this less severe type of ADHD
- ADHD-C (n=13)
- NOS (n=7)

LD (n=14)
- Dyslexia (n=25), Note: The vast majority here are dyslexic, hence our focus on the literature on this group.
- Dyscalculia (n=3)
- NOS (n=6)

Learning problems (n=20)

RM for all but n=4 who did JM all of these preschoolers diagnosed with ADHD were free of Rx.

Note: Additionally, they reran analyses excluding children on Rx, children who did JM (n=4) and children with dyslexia (n=3) and main and interaction effects remained.

Cogmed with children with Different Neurodevelopmental Disorders (ADHD, LD, Learning Problems) (Rording-Ragetlie, et al., 2016)

LD: Diagnosed by a registered clinical psychologist in the Netherlands (Dutch guidelines).

Learning problems: Without a DSM-IV diagnosis. “These children were experiencing academic achievement problems (lower grades than expected) and mixed neuropsychological impairments (memory- or attention problems in the classroom), as well as learning-related behavioral problems (Alloway & Alloway, 2010). Learning problems were diagnosed according to an official Dutch system that monitors academic achievement at school supplemented by the clinical opinion of the clinical psychologist and reports by parents and teachers about the child’s development.”

Exclusion criteria:
1) A medical illness requiring immediate treatment as this meant that participating in an intensive training would be too demanding; 2) A motor or perceptual disability preventing the subject from using the computer program; 3) No access to a personal computer with an internet connection at home or in school; 4) A lack of motivation (e.g., willingness on the part of the parents to participate, but not on the part of the child; or 5) A co-morbid (psychiatric) diagnosis.

Outcome Measures:
Dutch version of the ADHD rating scale (ADHD Vragen, Lijst, AVL, Scholte & Van der Ploeg, 2005). One index was for inattention and a second for hyperactivity/impulsivity. Completed by parents.

BRIEF (Behavior Rating Inventory of Executive Function checklist). Completed by parents.

WM capacity measured by two Cogmed components within the training program (Training index).
All three groups showed significant gains suggesting all groups profit from training:

- Inattention ($p<.0001$, $\eta^2=.57$
- Hyperactivity/Impulsivity ($p<.0001$, $\eta^2=.33$)
- BRIEF Total ($p<.0001$, $\eta^2=.27$
- WM ($p<.0001$, $\eta^2=.90$)

However, children with LD benefited less than the other groups on:

- Hyperactivity/impulsivity
- BRIEF Total

Also post-hoc Bonferroni analysis revealed that Inattention was statistically different between the ADHD and LD groups.

The hyperactivity/impulsivity was borderline statistically different between the LD and ADHD group also.

Possible Explanations: LD group needs more time to establish behavioral and EF-related improvements in daily life (Holmes, et al., 2009). 6 months post Cogmed post Cogmed gains in mathematics were found but no improvement found immediately following Cogmed (Holmes, et al., 2009). For the LD group the training may be primarily attention training not WM training. Holmes et al., 2009 found 37% of LD children in that study improved on attentional lices.

Other cognitive factors may play a critical role in LD: comprehension, listening and writing, phonological deficits and number module deficits.

"When looked at more closely, children in our study with learning problems showed a considerably higher baseline measurement regarding hyperactivity/impulsivity problems (meaning more problems) compared to children with LD. Perhaps the fact that there was less room for improvement in the LD group may explain the difference found in terms of benefit between these groups.” Or these differences may be statistical error or due to the measures used.

Limitations: “A major limitation of this study is the absence of a randomized design and a control condition. Therefore, the positive results in this study were not controlled for unspecific factors, such as invested time and attention, therapist interaction, or brain maturation.”

“Another limitation could be that the only WM measurement used in this study was the WM capacity improvement index measured by the Cogmed© computer program itself, which is not a pure clinical measure and is susceptible to practice effect.”

“... our study shows that Cogmed WM training might be (more) useful for children with relatively mild or subthreshold psychiatric disorders or learning disabilities at risk for a severe psychiatric disorder. This might prevent the development of a full psychiatric disorder or severe academic achievement problems. Our findings show that the “at-risk group” of children profit from a relatively short, but intensive Cogmed training program. Therefore, low cost interventions such as Cogmed WM training could possibly prevent the development of severe neuropsychiatric disorders.”

Rx use is low which is partly related to how the Dutch mental health care system works there. Psychological treatments are offered as the first line of tx for children with mild ADHD.
Van der donk, et al., 2014 supports notion implicit in this table: Far Transfer (red) is more likely among those with moderate severity & Rx is a factor to consider.

<table>
<thead>
<tr>
<th>Study</th>
<th>WM deficit</th>
<th>ADHD-C</th>
<th>ADHD-HI</th>
<th>RX%</th>
<th>LD</th>
<th>ODD/CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holmes &amp; Gathercole, 2013 (trial 1)</td>
<td>100%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Holmes, et al., 2009</td>
<td>100%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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</tr>
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<td>Dunning, et al., 2013</td>
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<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Bergman-Nutley &amp; Klingberg, 2014</td>
<td>Mainly Attention problems</td>
<td>Attentive problems/minor HI</td>
<td>Minor HI</td>
<td>NR</td>
<td>NR</td>
<td>Minor</td>
</tr>
<tr>
<td>Holmes &amp; Gathercole, 2013 (trial 2)</td>
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<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Dahlin, 2010</td>
<td>NR</td>
<td>33%</td>
<td>60%</td>
<td>0%</td>
<td>9.5%***</td>
<td>0%</td>
</tr>
<tr>
<td>Dahlin, 2013</td>
<td>33%</td>
<td>60%</td>
<td>22%</td>
<td>NR</td>
<td>22%</td>
<td>0%</td>
</tr>
<tr>
<td>Klingberg, et al., 2002</td>
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<td>100%?</td>
<td>NR</td>
<td>43%</td>
<td>NR</td>
<td>0%</td>
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<td>Klingberg, et al., 2005</td>
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<td>75%</td>
<td>0%</td>
<td>0%</td>
<td>NR</td>
<td>0%</td>
</tr>
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<td>Hovik, et al., 2013/Egeland, 2013</td>
<td>NR</td>
<td>100%</td>
<td>0%</td>
<td>69.6%</td>
<td>NR</td>
<td>NA/0%</td>
</tr>
<tr>
<td>Green, et al., 2012</td>
<td>42%</td>
<td>42%</td>
<td>17%</td>
<td>67%</td>
<td>0%</td>
<td>NR</td>
</tr>
<tr>
<td>Van Dongen-Boomsma, et al., 2014</td>
<td>7.7%</td>
<td>80.8%</td>
<td>11.2%</td>
<td>0%</td>
<td>3.8%/0%</td>
<td></td>
</tr>
<tr>
<td>Beck et al., 2010</td>
<td>NA</td>
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<td>29%</td>
<td>NR</td>
<td>61%</td>
<td>NR</td>
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<tr>
<td>Chacko, et al., 2013</td>
<td>34%</td>
<td>66%</td>
<td>0%</td>
<td>27%</td>
<td>NR</td>
<td>50%/9%</td>
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<td>Gropper, et al., 2014</td>
<td>-</td>
<td>51%</td>
<td>NR</td>
<td>NR</td>
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<td>57%</td>
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<tr>
<td>Gray et al., 2012</td>
<td>-</td>
<td>100%</td>
<td>NR</td>
<td>98%</td>
<td>100% Severe 100%/0%</td>
<td></td>
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</table>

Far Transfer Challenge.

What is the mechanism of change? Limiting factors?

1. Leveraging WM partly hinges upon individual differences like "mindset", growth-oriented VS static.
2. Leveraging relates to student motivation.
3. Leveraging relates to the extent to which Cogmed training is optimized "Cogmed Plus".
   Is Near Transfer Needed?  
   - Domain specific knowledge or skills (vocabulary)?
   - Domain general skills (processing speed)?
   - Rate of learning
   - Following Instructions
   - Executive Functions

Far Transfer Challenge.

Is Near Transfer Needed?  
- Domain specific knowledge or skills (vocabulary)?
- Domain general skills (processing speed)?
- Rate of learning
- Following Instructions
- Executive Functions

Far Transfer End Goal:
- Reading comprehension
- Math skills
- Language development
- On-task behavior

The Far Transfer Challenge.

Skill behavior "Far Transfer"
- Reading comprehension
- Math skills
- Language development
- On-task behavior

Generalized effects "Near Transfer"
- Rate of learning
- Reduced Cognitive Failure
- Following Instructions
- Attention/Concentration

Executive functions
- Working memory
- Planning
- Initiate
- Task monitoring
- Organize

Is Rx needed to optimizie Cogmed effects?

May need domain specific skills, may need improved domain general executive functioning skills.
Cogmed & Inattentive Children with learning problems

WM training effects on reading in ADHD or inattentive Children with learning problems (2)
(Dahlin, 2010)

<table>
<thead>
<tr>
<th>Date</th>
<th>WM tasks</th>
<th>WM deficit</th>
<th>ADHD-1</th>
<th>ADHD-2</th>
<th>Rx%</th>
<th>LD</th>
<th>ODD/CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dahlin, 2010</td>
<td>NR</td>
<td>33% diag.</td>
<td>60%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>9.5%***</td>
</tr>
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Population: special needs children, ages 9 – 12 years
N = 57 (n = 42 in treatment group and n = 15 in control group [special needs class])
Diagnosed with ADHD or inattention and with co-morbidity of learning problems.

Design: Active control, Randomized, Blindfold, Test-retest
T1 = Baseline, T2 = 5-6 week follow up, T3 = 6-7 month follow up
Treatment group improved significantly on outcome measures:
1) Visuo-spatial and verbal WM (Span Board; WAIS-NI & Digit Span; WISC III) (T2)
2) Reading comprehension (Reading narrative texts & answering questions) (T2 & T3)

Examined the relationship between working memory and reading achievement in 57 school children with special needs.

Special needs: 33% had ADHD diagnosis, 60% rated inattentive by teachers & general learning problems

Significantly improved untrained working memory tasks, nonverbal problem solving & reading comprehension. Effect size for reading comprehension was d=91, it was substantial.

Take home: Children with attention with special education needs and attention problems improved significantly on untrained working memory tasks, nonverbal problems solving and reading comprehension with WM training group.
WM training effects on reading in ADHD or inattentive Children with learning problems (2)  
(Dahlin, 2010)

<table>
<thead>
<tr>
<th>Time</th>
<th>Treatment group</th>
<th>Center group</th>
<th>Effect size (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>T1</td>
<td>1.00</td>
<td>0.90</td>
<td>1.00</td>
</tr>
<tr>
<td>T2</td>
<td>1.00</td>
<td>0.90</td>
<td>1.00</td>
</tr>
<tr>
<td>T3</td>
<td>1.00</td>
<td>0.90</td>
<td>1.00</td>
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</tbody>
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Study II:  Dahlin (2013) found that WM and basic number skills were highly related. The performance of boys in the treatment group improved more than boys in the control group on basic number tests at both post-tests.

Study III: Basic skills assessed three years later (T4) are reported. Gains in reading Comprehension, VWM/LSTM, central executive WM maintained at 3 years.

Inattentive Children w/learning problems: WM training generalizes to Reading Comprehension & Basic Number Skills & lasts 3 years  
(Dahlin, 2013)

<table>
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<th>Study</th>
<th>WM training generalizes to Reading Comprehension &amp; Basic Number Skills &amp; lasts 3 years</th>
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WM training generalizes to Reading Comprehension & Basic Number Skills & lasts 3 years  
(Dahlin, 2013)

Study II: n=27 students. 18 treatment (9 with ADHD, 9 control (4 with ADHD). Some had dyslexia.

Psychologists interviewed the parents of students in the treatment group for 30-40 minutes to ensure they did have attention difficulties.

Parents completed ODD ratings.

Assessments by teachers and psychologists from each school formed the basis for participation in the study.

Basic number skills:

Addition & Subtraction verification tasks. In two minutes, the student determines whether equations have been calculated correctly.

Basic Number screening test: BNST (Gillham & Hesse, 2001) 30 different tasks in mathematics, including the four basic arithmetic operations, grouping and completing series.

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Basic Number screening test: BNST (Gillham & Hesse, 2001) 30 different tasks in mathematics, including the four basic arithmetic operations, grouping and completing series.
Study II: BNST was significant at T2 (post-Cogmed) but not T3 (6-7 months post-Cogmed) for the tx group.

NOTE: Girls were few in number and performed significantly poorer than boys on several tests so analyses were only repeated for boys.

The re-analysis showed significant improvement in the BNST at T2 (treatment effect = p < .05, d = 0.74) as well as at T3 for the boys (treatment effect = p<.05, d = 0.90), but not in addition or subtraction.

The experimental group’s results from the different test sessions were computed using Cohen’s d. The effect on WM tests (Span board) was high (forward, d = 1.05, backwards, d = 0.93)

The conclusion drawn is that mathematics and WM are related. Boys aged 9 to 12 years seem to benefit from WM training by improving their performance on both the WM test and the mathematics test (BNST).

Study III: n=27 students. It was decided to ask 2/3 of the control group (n=10) and twice as many from the treatment group (n=20) to complete the reading and mathematics measures once again at 3 years follow-up. This resulted in a control group of 9 students (3 female) and 2 with ADHD and 18 (3 female (4 with ADHD) in the treatment group. Financial limits prevented follow-up with all 57 students.

3 students lost: 1 boy due to ODD, 1 girl due to low IQ. One boy in control group did Cogmed between T2 and T3 so he was removed.

Effect size notes: “An effect size (d) of 1.0 for a subject indicates an increase of 1 SD (standard deviation). According to Hattie (2009), this signifies an increase equivalent to two to three years of development and a 50% increase in development speed. If d = 1.0 in an intervention study, it effectively means that the treatment group outperforms as much as 84% of the control group participants, which takes into account differences in the form of SDs between tests outlining statistical significance.”

Study III: VSWM: Significant at T2 (directly after training) & T3 (6-7 months after training).

Reading Comprehension: Entire experimental group significantly improved at T2, T3 and T4 (3 years follow-up) in reading comprehension.

Among boys: At T4: Significant improvements in VSWM (Span board backwards), VS-STM (Span board forward), significant improvements in Central executive WM: Attention DSM-IV, Questions 1-9, rated by parents and teachers.

Significant improvement effect sizes in Reading comprehension (1.09) and basic number skills in boys, subtraction (.94), basic number test (.75). Also, reading comprehension and number skills were related to WM measures.

ADHD or not: No difference was found in training effect whether with or without the diagnosis.
WM training generalizes to Reading Comprehension & Basic Number Skills & lasts 3 years
(Shallice, 2000)

<table>
<thead>
<tr>
<th>Follow-up Statistics for boys</th>
<th>T2-T1</th>
<th>T3-T1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Span board forward</td>
<td>1.25</td>
<td>1.09</td>
</tr>
<tr>
<td>Span board backward</td>
<td>1.05</td>
<td>.83</td>
</tr>
<tr>
<td>Digit forward</td>
<td>.57</td>
<td>.44</td>
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<tr>
<td>Digit backward</td>
<td>.87</td>
<td>.36</td>
</tr>
<tr>
<td>Raven</td>
<td>.45</td>
<td>.52</td>
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<tr>
<td>Addition</td>
<td>.31</td>
<td>.56</td>
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<tr>
<td>Subtraction</td>
<td>.10</td>
<td>.23</td>
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<tr>
<td>Number skills</td>
<td>.26</td>
<td>.56</td>
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<tr>
<td>Reading comprehension</td>
<td>.67</td>
<td>.76</td>
</tr>
<tr>
<td>Word Reading</td>
<td>.22</td>
<td>.35</td>
</tr>
</tbody>
</table>

Children Identified by a lack of educational achievement who arguably in our context may fit the group categorized as having “learning problems”

Children with poor Educational Achievement
(Trial 2, Holmes & Gathercole, 2013)

<table>
<thead>
<tr>
<th>Trial 2</th>
<th>WM tasks</th>
<th>WM deficit</th>
<th>ADHD-I</th>
<th>ADHD-C</th>
<th>ADHD-HI</th>
<th>Rx</th>
<th>LD</th>
<th>ODD/CD</th>
<th>NR</th>
<th>NR</th>
<th>NR</th>
<th>NR</th>
<th>NR</th>
<th>100%</th>
<th>NR</th>
</tr>
</thead>
</table>

Children with poor Educational Achievement (Trial 2, Holmes & Gathercole, 2013)

nr-50 children ages 9–11 low academic performance from a cohort of 256 Year 5 and 6 children attending middle school in South East England. Selections based on raw scores in English and math from teacher assessments administered at the end of the previous year.

English assessed reading, writing, speaking and listening skills. Math assessed the ability to use and apply math, complete tests of number and algebra, shape space and measures and handling data.

N=25 from Year 5 (age 9 years, 5 months, 16 boys) and 25 from year 6 (age 10 years, 6 months, 13 boys). These children had the lowest teacher assessment scores of their cohorts. They were matched with 50 children based upon age, gender and performance on the teacher assessments from the previous cohorts of children in year 5 and 6.
Data are presented separately because year 5 and year 6 have distinct status in the UK state education system. SAT’s are required in year 6 and optional in year 5.

The year 5 group was trained as one group of 25 supervised by the head teacher and a classroom assistant. (Whole class)

Year 6 was trained in two smaller groups (n=13, n=12) supervised by the same staff at the end of the school day.

| Children with poor Educational Achievement (Trial 2, Holmes & Gathercole, 2013) |
|-------------------------------|-----------------|

Children in Year 5 who completed training made significantly greater gains in math than the comparison group.

Children in Year 6 who completed training made significantly greater gains in English and Math.

Of the trained group at the end of Year 6 84% reached the nationally expected levels of attainment in English at the end of Year 6 compared with 72% of the comparison group.

Academic attainment was not related to baseline attainment.
10-12 year old ADHD children make and maintain significant gains in WM for 8 months. RCT

**RCT results:** Systematic training resulted in long term gains (8 months).
Evidence for both domain-general and domain-specific models.

- n=67 children 100% with combined type ADHD ages 10-12.
- 41 Rx stimulant (MPH) + 5 atomoxetine (Straterra) + 1 Risperidone. 70% on Rx

**Design:** Randomized, Placebo controlled Trial, RCT. Treatment vs. treatment as usual. 8 month follow up. Control group received special education treatment as usual & health care follow up.

**MEASURES:** 6 measures of each form of WM, divided into auditory WM, visual WM, and Manipulation WM

**RESULTS:** All treatment subjects significantly improved on all measures of WM. Improved significantly more on Visual WM than auditory WM. Manipulation WM gain remained after controlling for increase in simple storage.

Gains were found in both domain general and domain specific areas.

**Study WM deficit ADHD-I Attention problems ADHD-C ADHD-HI Rx% LD ODD/CD**

```
Hovik, et al., 2013 - 0% 100% 0%
```

**Cogmed Training results in improved psychomotor speed & reading. RCT (Same subjects as Hovik, et al., 2013)**

**N=67 children diagnosed with ICD-10 Hyperkinetic Disorder 100% ADHD Combined type, randomly selected into a control group or training group. 70% on Rx, RCT. Control group received special education treatment as usual & health care follow up. Ages 10-12.**

**Exclusion criteria:** 1. IQ below 70. 2. Comorbid diagnosis of Pervasive Developmental disorders, Tourette’s disorder, evidence of psychosis or Bipolar disorder and Conduct disorder.

**Measures:** Battery of NP tests, measures of mathematics and reading skills.

**Results:** Psychometric or processing speed improved. Reading improved. Reading was improved in both speed and quality of text reading and word decoding quality improved.

**Normalization before Cogmed:**
- No differences between groups regarding medications were found.
- The majority of subjects performed in the normal range on the CCF-II before Cogmed.
- Children referred for medications may be more impaired.
- They hypothesized that children who have optimized their behavior due to Rx may show less treatment effect.

**Implications:** Control for medication.
<table>
<thead>
<tr>
<th>WM deficit Children: Transfer increased Linearly with amount of training time &amp; Correlated with improvement on trained tasks. WM, FI &amp; Math Improved</th>
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<tbody>
<tr>
<td>Bergman-Nutley &amp; Klingberg, 2014</td>
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<thead>
<tr>
<th>Study</th>
<th>WM-deficit</th>
<th>ADHD-I</th>
<th>ADHD-C</th>
<th>ADHD-HI</th>
<th>LD</th>
<th>ODD</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bergman-Nutley &amp; Klingberg, 2014</td>
<td>100%</td>
<td>Mainly Attentive problems</td>
<td>Attentive problems</td>
<td>Minor HI</td>
<td>NR</td>
<td>NR</td>
<td>Minor</td>
</tr>
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</table>

WM deficit Children, ages 7-14, mean age 11.1 years, all had WM deficits. Majority were diagnosed with ADHD, but it was not verified in the study. Based upon the rating scale noted below children had "mainly inattentive problems (score of 16) and minor problems with hyperactivity (score of 8) and ODD (score of 6)."

n=104 Typically developing children, aged 7-15. This group took same transfer tasks at the same weekly intervals for 5 weeks. They did not train.

Assessments: Disruptive Disorder Behavior Checklist, parent ratings, before training. Transfer tests administered once a week for 5 weeks:

Working memory: "odd one out" (OOO) identify which shape is the odd one out and remember its location. Based upon the AWMA, 2007

Following instructions: digitized from classroom analog test developed by Gathercole, et al., 2008), practice trials with one and two items and then begins with first task of 2 items; test concluded when two items at the same level are incorrect, (span task)

Mathematics test: See next slide.

WM deficit Children: Transfer increased Linearly with amount of training time & Correlated with improvement on trained tasks. WM, FI & Math Improved

Mathematics test: The mathematics test was a speeded arithmetic test where the participants had to solve mental arithmetic problems (addition and subtraction) with two or three terms and a sum less than 20, excluding duplicate terms and numbers with 0 in them. As many problems as possible were to be answered during 1 min. The scoring was the sum of the correctly answered trials after subtracting the number of mistakes multiplied by 0.33 (so that random performance would give a score of 0). This might be considered a test of math proficiency given the fact that it is a timed test.

Standard training format: trained 5 days/week for 5 weeks.

Compliance was very high with a mean of 24.89 days trained & 88% completed all 5 tests. Training was done during the summer of 2012.

Realize: "Transfer increased Linearly with amount of training time & Correlated with improvement on trained tasks."

WM, FI & Math significantly improved

Take note that changes begin to be registered at about 3 or more weeks into training.

As such the role of the coach in supporting the motivation of the trainee is very important.
WHY THIS STUDY MATTERS:

WM is impaired in subjects with dyscalculia & it is correlated to math performance in the general population. Performance on WM tests is predictive of future math performance. Math underachievement is associated with academic underperformance and higher risk for unemployment.

“Studies investigating the effects of WM training on mathematics have thus far presented mixed results regarding such transfer (Gray et al., 2012; Dunning, Holmes, & Gathercole, 2013; Holmes & Gathercole, 2013).”

“The inconsistent results of WM training on mathematics could be due to: (1) a true lack of effect or that only certain aspects of mathematics are affected; (2) that effect occurs not directly after training but later, as a result of improved WM capacity in combination with instruction; or (3) that the effect size is small, and the existing studies include too few subjects to detect a significant effect.”

<table>
<thead>
<tr>
<th>Test</th>
<th>Improvement</th>
<th>Measure</th>
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<tbody>
<tr>
<td>WM</td>
<td>Improvement</td>
<td>Linear</td>
</tr>
<tr>
<td>FI</td>
<td>Improvement</td>
<td>Minimal</td>
</tr>
<tr>
<td>Math</td>
<td>Improvement</td>
<td>Small</td>
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</tbody>
</table>

Improvements in FI were linear and showed minimal test-retests in the control group. In OOO and the mat test there were test-retests effects in the control group at T2 and T3 after which they leveled off. With all 3 measures the maximal difference between training and control group was seen in the final testing (T5).

EFFECT SIZES:
The effect for WM (OOO) was medium to strong (d = .67).
The effect size for FI was strong: (d = .90).
The effect-size for math was small (d = .20).
DESIGN: Wait list control. Not blinded (Cannot claim causality.)
n=62, college students, ages 19-54.
Registered with student services with a confirmed diagnosis of ADHD & LD

BESD Binomial Effect Size Display (BESD) calculation was used to compare changes in effect size of WM capacity.

CFQ: Cognitive Failure Questionnaire was used at a measure of generalization but is also considered a measure of “ecological effects”.

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ADHD in College: ADHD/LD in college are a unique subgroup. On the one hand, they are likely to have missed substantial skill development over their academic career. As such, expecting academic achievement to improve would be quite challenging. On the other hand as ADHD/LD who made it to college they are doing comparatively well. So they would be both relatively high-achieving as well as possibly to have gaps in their development.

Expectations: Improving “learning capacity” after expected years of lagging behind would be an optimistic outcome. Then academic skill remediation with scaffolding would be expected to have a notably greater impact.

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RESULTS:
Cogmed resulted in significantly improved VWM (WAIS), VSWM -(CONTAB).
Gains maintained at 2 month follow up. Also, self-reported fewer ADHD symptoms (ADHD Self Report Scale) and fewer cognitive failures post program. At 2 months they continued to report fewer cognitive failures.

Using Binomial Effect size display (BESD) 47% difference between groups, BESD 28% reduction of symptoms, cognitive failure questionnaire 25% reduction.

Index scores predicted WM improvement on CONTAB, ASRS, CFQ. In other words students cannot just go through the motions.

BETTER EFFORT = BETTER RESULTS
ADHD/LD College Students Self-reported changes post Cogmed suggest ecological improvements. (Gropper, 2014)

THE STUDENTS CONCLUSIONS (Ecological effects):

Majority noticed an improvement in recalling verbal information (e.g. phone numbers, appointments, names).

Improvement in verbal memory allowed students to learn and retain information from lectures and books without rereading over and over again.

Several students reported that they could better sustain attention and feel alert for longer periods of time.

Some reported that they did NOT improve in time management or organizational skills, but there were no substantial changes in these areas. The argument for scaffolding makes sense.

Overall the feedback was positive.

However, the authors conclude that a causal link between Cogmed and these changes cannot be assumed.

The study by Gray et al, 2012 was the most severely debilitated group of ADHD-C/ODD-LD Children to do Cogmed.

<table>
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<th>Study</th>
<th>WM deficit ADHD-C ADHD-I Attention problems ADHD-HI Rx% LD ODD/CD</th>
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<tr>
<td>Gray et al., 2012</td>
<td>NR</td>
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</table>

DESIGN: RCT, control group received math-training. All students were in a residential treatment facility in which they received Complimenting factors were that both groups were in a school with extensive remedial social work with psychopharmacological treatment resulted in gains for both groups of children. This included attention, reading, math and behavior.

Results: Cogmed training resulted in significant but small gains on verbal (Eta=.13) and visuo-spatial WM (Eta=.08) but not on teacher or parent behavioral ratings or academics compared to group training on math tasks. On a subset of WM criterion measures upon which this group improved significantly compared to the control which was a math-training group.

n=60, (52 male, 8 female), ages 12 to 17, average age=14.2 tx, average age of control=14.4. (Peer groups)

Gray et al. (2012) studied a group of treatment resistant adolescents with combined severe LD and ADHD, as well as majority of children (57 - 77%) falling below 16th percentile for WM.

UNUSUALLY ‘Treatment-resistant’ SEVERE SUBJECTS:

Residential school required both ADHD/LD along with severe problems in behavior and learning AND they had to have already had a poor response to both medication treatment and special education treatment. They had to have failed previous interventions.

Oppositional Defiant Disorder (ODD): All were at or above the 90th percentile on ODD as rated by both parents and teachers.

Learning disabilities: Severe learning disabilities were severe with “Notably, all academic scores were more than two standard deviations below the mean (WRAT-4)” at baseline.

Design Challenges: The comparison group was receiving a math intervention that the control group did not get. The notion that the Cogmed group would exceed them in improving in math seems highly unlikely.
The study by Gray et al, 2012 was the most severely debilitated group of ADHD-C/ODD/LD Children to do Cogmed.

**Key Finding**: They found that “those who showed the most improvement on the WM training tasks at school were rated as less inattentive/hyperactive at home by parents.”

Greater progress within the program resulted in greater improvement on inattentive/hyperactive by parents.

This theme has arisen in other studies that there is a trend toward greater increases on the training index as the training task results in better results. A trend like this was seen in the van-Dongen-Boomsma et al. study.

Key Finding: The training index significantly contributed to an ADHD rating scale and the BRIEF by the teacher, but there were not significant group differences.

**Dosing hypothesis**: One wonders whether subjects needed more training time to accomplish greater gains.

“A possible explanation for these findings is that longer and more intensive training may be required to ameliorate severe difficulties in WM” (Gray, et al., 2013). This is a matter of dosing which in other areas of computerized cognitive training has been explored in more depth.

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**Predictors & Moderators of Treatment Outcome in Cognitive Training for Children with ADHD**

(Van der Donk, et al., 2016)

n=98, children ages 8-12.

Do clinical variables and initial cognitive abilities predict or moderate far transfer treatment outcomes of cognitive training?

- Groups randomly assigned to Cogmed or “Paying Attention in Class” a new cognitive training.

**Outcomes measures**: Neurocognitive assessment, parent & teacher ratings of executive functioning (EF) behavior and academic performance.

**Predictor variables**: Rx, comorbidity, ADHD subtype, initial verbal & (VWM) visual (spatial) working memory (VSWM).

**Results**: Subtype of ADHD predicted & moderated Parent & teacher ratings of EF.

**Conclusion**: Cognitive training can be beneficial for certain subgroups of children with ADHD, individual differences should be taken into account in future trials.

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**Breaking down the results**

**Cogmed** resulted in an improvement on VSWM for all groups that was greater than the control group. Time effects were found on several variables.

**Rx**: Impacted upon VSWM: Directly after Cogmed children on Rx benefited the most from Cogmed in terms of VSWM which was maintained at follow up. Children without Rx also benefited with improved VSWM at the conclusion of Cogmed, but this was not maintained at follow up.

For 45 children on Rx, type of Rx was changed for 10 at follow up.

For 40 who did not use Rx during Cogmed, 4 started Rx at follow up.

Comorbidity adversely affected far transfer: Predicted effect on word reading accuracy. Children without comorbidity increased on word reading accuracy directly after treatment those with comorbidity decreased in accuracy.
### ADHD Subtype as Predictor of Treatment Outcome in Cognitive Training for Children with ADHD, Near Transfer

(Van der Donk, et al., 2016)

**ADHD Subtype:**
- Predicted & Moderated Parent Ratings of EF:
  - ADHD-C: BRIEF behavioral regulation index rated by parents & teachers showed a decrease in behavioral regulation problems both directly post Cogmed and at follow up.
  - ADHD-I: Steep decrease behavioral problems post Cogmed, but increase at follow up.

**Teacher Rating of Beh. Reg. Index & Metacognitive Index:**
- ADHD-C: Decrease of problems over time (both post and follow up) & no difference between intervention groups.
- ADHD-I: Decrease in problems over time.

**Summary:** ADHD-I group benefitted more both short and long term. In short-term ADHD-I benefitted more from Cogmed in general in terms of parent and teacher rated behavioral regulation problems. Long-term ADHD-I benefitted on teacher rated behavioral regulation, metacognitive problems. ADHD-C still showed more problems than children with ADHD-I subtype over time.

**Children in PAC intervention:** Increase of problems at follow up.

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### Initial Cognitive Abilities, subtype & comorbidity as Predictors of Treatment Outcome in Cognitive Training for Children with ADHD.

(Van der Donk, et al., 2016)

**Initial VSTM:**
- Children ‘below average’ and ‘average’ showed improvements over time.
- Children ‘above average’ showed a decrease in performance over time, but were still higher than the other groups at all time points.

**Subtype of ADHD & Comorbidity:** Predicted word reading accuracy.

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### ADHD Subtype as Predictor of Treatment Outcome in Cognitive Training for Children with ADHD, Far Transfer.

(Van der Donk, et al., 2016)

**ADHD-C:** Improved on word reading accuracy directly post Cogmed and was maintained at follow up.

**ADHD-I:** Decrease in word reading accuracy post Cogmed, but improved at follow-up & even outperformed ADHD-C children. **THIS IS SURPRISING AND FAIRLY UNPREDICTABLE.**

This finding highlights an element of unpredictability in the change process and the timing of change.

The overall trends of data in this study generally supported our hypotheses based upon previous data.
Thank you!