


Pearson


Working Memory Training And Evidence-Based Interventions for ADHD



Charles Shinaver, PhD
Peter Entwistle, PhD


May, 2017


 Pearson



Pearson

Presenter: Charles Shinaver, PhD
Cognitive Consultant
(888) 748-3828, x110
(800)627-7271 x 262355
(317) 641-7794
charles.shinaver@pearson.com

Chat box:
Peter Entwistle, PhD
Cognitive Consultant
888-748-3828, x111
202-333-3210
Peter.entwistle@pearson.com




 Pearson



Agenda

- How does Working Memory, the Target of Cogmed, relate to ADHD and learning?
- Developmental Trajectories for ADHD into adulthood.
- Factors to consider in evaluating interventions severity, comorbidity and medication status.
- Intriguing differences between ADHD-C vs. ADHD-I.
- Rx Treatment highlights.
- Behavioral treatment highlights.
- Working Memory training highlights including combined treatment of Rx & Cogmed.
- Temperament as a consideration.
- New directions for research, education & clinical practice.
- Summary

 19

Disclaimer

I speak today as an employee of Pearson, but I do not speak "for" Pearson. This is not a "Pearson" position. However, I am a clinical child psychologist training in the scientist practitioner model. I have worked with ADHD assessment and treatment for 20 years. I am also an author of relevant journal articles and book chapters.

Today's intended audience is mental health professionals and educators. Parents may learn from this but it is likely to contain unfamiliar content as well.

Meta-analyses will be considered, but they flatten and ignore differences in severity and comorbidity which we consider to be a clinical, educational and research shortcoming. It confounds the findings of meta-analyses. Remember the significance of the "n of 1".

I have had family members and clients use all the approaches I will discuss today. I believe that they all have merit. They all have an impact. However, I do not believe than any one of them is "THE ANSWER". However, today we will consider some data that suggests a **combination of treatments** may be a "**better answer**" than any one treatment alone. ADHD is a heterogeneous disorder with varying levels of severity and comorbidity. The converse of varying levels of severity and comorbidity might be captured in considerations of "**temperament**", or more specifically "**effortful control**" which we will discuss today. Clinical and educational nuance and sophistication is needed to help these patients which is rarely captured in research like meta-analyses.

There are other treatments for ADHD for which meta-analyses have been completed. My wise colleague, Peter Entwistle, PhD suggested I cut this down so as to reduce the likelihood of overwhelming the audience. If enough interest is garnered another webinar might consider a few other 'alternative approaches to the treatment of ADHD'.



1

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

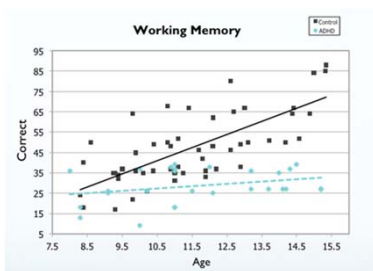
Delegates to different parts of our brain to take action - shifting

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.




Westerberg et al. (2004). Visuo-spatial working memory: a sensitive measurement of cognitive deficits in ADHD. Child Neuropsychology 10 (3) 155-61.



WM deficits correlate with Reading Comprehension Problems: Meta-analysis.
(Caretti, et. al., 2009)

Good comprehenders vs poor comprehenders:
 "...memory tasks that are demanding in terms of **attentional control and that require verbal information processing** are best at distinguishing between" between these two groups.
 "...**suggesting that both domain-specific factors as well as general factors of working memory contribute to reading comprehension performance.**"



Prd Li

Pearson

Visual Spatial (VS) WM & VS Short Term memory PREDICT Math achievement.
(Bull et al, 2008)

For 4 year old children WM & ST memory along with EF (executive functioning) **predicted 1st grade and 3rd grade achievement.**

BETTER DIGIT SPAN (verbal working memory) & EF skills provided an immediate head start in math and reading that was maintained through the first 3 years of school.


Visual spatial working memory and visual spatial short term memory predicted math achievement at each time point.

EF (executive functioning) skills predicted learning in general.

Pearson

Growth in WM predicts better math problem solving
(Swanson, et. al., 2008)

n=353 at risk elementary school children 1st-3rd grades.
 Assessed children at risk for serious math problems.
 Is growth in working memory an important predictor of children's problem solving in math? YES.
Growth in WM is an important predictor of children's problem solving beyond the contribution of reading, calculation skills, and individual differences in phonological processing, inhibition, and processing speed.



Pearson


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 these struggles: A distinct trajectory of less academic achievement.



 1

ADHD Developmental Trajectory: Adversity in Adults with history of Childhood ADHD.

(Barbareis, et al, poster session SDBP 2011)

Research Identified **ADHD cases** in a population based **birth cohort** from 1976-1982 **birth cohort (n=5699)**, Ages 5 to 19.


Vital stats for **367 ADHD cases** who did not deny access to their medical records for research. Number of deaths compared with expected number derived from state census data to construct a standardized mortality ratio (SMR).

***7 deaths of 367 ADHD vs. 2.14 expected. SMR of 3.3 (95% CI 1.3-6.7; p<.001)**

*Mean age of death: 22.19, cause of death accidents (n=3), suicide (n=3).

ADHD cases were invited to participate in a prospective follow up study. (n=232 ADHD, mean 26.9 years; 167 male, 65 females; control(n=335, mean 28.6 years; 210 males, 125 females).

• Not Graduated from high school:	17.7% vs. 6.0%; (p<.01).	Ratio: 2.95/1
• Degree beyond high school:	37.1% vs. 67.5%; (p<.01).	Ratio: 1/1.81
• Married:	26.7% vs. 45.7%; (p<.03).	Ratio: 1/1.71
• Unemployed:	9.9% vs. 5.1%; (p<.09).	Ratio: 1.91/1
• Fired from a job:	50.9% vs. 21.2%; (p<.01).	Ratio: 2.4/1
• Less well paid:	\$20,000 vs. \$30,000 (p<.01)	Ratio: 1/1.5

 1

ADHD Developmental Trajectory: ADHD Symptoms Predict Social Functioning in High School.

(Anixi, et al., 2011 Plenary Session Abstract SDBP)

Hyperactivity predicted passive ignoring at (p<.001) level. Attention problems were a significant predictor of passive ignoring. Paralleled self-reported social outcomes.


Getting ignored in high school...not a pleasant experience...

Core ADHD symptoms differentially predicted an adolescent's location in the social network and peer-perceived acceptance/exclusion.

Increasing both hyperactivity and inattention was associated with increased risk of active social exclusion.

Getting excluded is as bad or possibly worse.

This data suggest the need for targeted interventions to address social skills development of adolescents with ADHD.

 1

ADHD trajectory into Adulthood.
Consider **Work: Unemployment & Underemployment**

A longitudinal national sample with sibling pairs found that employment reduction among those with ADHD was "between 10 and 14 percentage points, the *earnings reduction is approximately 33%* and the *increase in social assistance is 15 points*" (Fletcher, 2014). Clearly ADHD adults are a group that is at risk for underemployment and unemployment.

Clinic referred sample of adults with ADHD:
•22.2% worked as their source of income (Bjervan, et al., 2012).

General population:
•72% work for income (Bjervan, et al., 2012).

KEY POINT: *Higher inattentive ratings were associated with a lower level of employment.* (Bjervan, et al., 2012).



Risks of childhood ADHD and long-term outcome of arrests, convictions, and incarcerations.
(Mohr-Jensen & Steinhausen, 2016)

15,442 individuals with childhood ADHD.

Childhood ADHD was significantly associated with
adolescent and adulthood arrests (RR: 2.2, 95% CI: 1.3-3.5),
convictions (RR: 3.3, 95% CI: 2.1-5.2) and
incarcerations (RR: 2.9, 95% CI: 1.9-4.3).

Individuals with ADHD had a younger age at onset of antisocial involvement and an increased risk of criminal recidivism."

Note: RR= Relative risk. In statistics and epidemiology, **relative risk** or risk ratio (**RR**) is the ratio of the probability of an event occurring (for example, developing a disease, being injured) in an exposed group to the probability of the event occurring in a comparison, non-exposed group.

https://en.wikipedia.org/wiki/Relative_risk



114

ADHD Adults & Prison:
One way to reduce its likelihood: Rx.
(Lichtenstein, et al., 2012)

Intriguing and massive population (n=25,656) study in Sweden.

"...among patients with ADHD who were taking medication there was a significant 32% reduction in the criminality rate for men and a 41% reduction in women."

Crime reduction notable even when:
Different drugs (stimulants vs nonstimulants) were used to treat ADHD and
Different crimes were tracked (violent vs. non-violent).

The reduction in criminality ranged from between 17%-46%.

Critical first step: adults are thoroughly assessed and properly diagnosed and encouraged to obtain proper treatment.

Treatment may include medication which will need to be effectively monitored.

Rx can help, but they are likely to need more.



1


“Cogmed Working Memory Training: Reviewing the reviews”
 (How to think about factors that limit the effects of interventions.)
(Shinaver & Entwistle, 2014)

Argument: Combined type ADHD (ADHD-C) is a more **severe** disorder than ADHD inattentive type (ADHD-I).

The impact of this distinction has been underestimated in the Cogmed research literature.

Comorbidity is a critical factor to consider when evaluating effects of any intervention. ADHD-C has more severe comorbidity. ADHD-I has more comorbid learning issues.

Control for medication effects (Rx), which can get complicated as ADHD-C and ADHD-I may have differential responses to Rx.



Pearson 116

We were onto something: Predictors of persistence of ADHD into adulthood,
 A systematic review of the literature and meta-analysis.
(Caye, et al., 2016)

26,168 abstracts reviewed and selected 72 for full-text review.
 16 studies used: 6 population-based retrospective samples and 10 clinical follow-ups.

Persistence of ADHD into adulthood was predicted by:

Severity of ADHD	(OR 2.33, 95 % CI = 1.6–3.39, $p < 0.001$),
Treatment for ADHD	(OR 2.09, 95 % CI = 1.04–4.18, $p = 0.037$),
Comorbid conduct disorder	(OR 1.85, 95 % CI = 1.06–3.24, $p = 0.030$),
Comorbid major depressive disorder	(OR 1.8, 95 % CI = 1.1–2.95, $p = 0.019$).

OR =Odds ratio.

Implication: More complicated cases of ADHD and greater comorbidity means ADHD is more likely to persist into adulthood.

Pearson 117

Intriguing differences between ADHD-C & ADHD-I.

Several studies establish **ADHD-C is more severe than ADHD-I**. Here are a couple:

1. Bilgic, et al., (2006) found more conduct disorder and earlier referral ages for ADHD-C.
2. McConaughy, et al., (2009) found ADHD-C worse in all these areas: (1) *Attention Problems*; (2) *Oppositional*; (3) *Attention Deficit/Hyperactivity Problems* scale; (4) *Inattention* subscale; (5) *Hyperactivity-Impulsivity* subscale; and (6) *Externalizing*.

ADHD-I patients struggle more with academic problems (Wolraich, et al., 1998).

Recall also that higher inattentive ratings were found to be associated with a lower level of employment (Bjervan, et al., 2012).

ADHD-I more common in girls and in adolescents and adults (Dunn & Kronenberger, 2003).
ADHD-I among those more likely to show minimal or no response to Rx. (Hale, et al., 2005)

Inattention more frequently persists into adulthood. (Willcutt, 2012, meta-analysis)


This suggests Cogmed is more relevant as those with ADHD age.

Pearson 118

Medication Tx of ADHD in children, *highlights of positive findings: Reduced Core ADHD symptoms.*

Search: ADHD treatment & meta-analysis (not exhaustive)

- Recent literature review found **13 relevant meta analyses of this approach.**
- Stimulant treatment of ADHD is the most researched & likely the most clinically utilized in the USA.**
- Consistent positive finding of improved rating scale data from parents and teachers for the core symptoms of ADHD and general behavior problems** (Shaw, 2016).
- As noted previously Lichtenstein, et al., (2012) found **reduced criminality** from "...among patients with ADHD who were taking medication there was a significant 32% reduction in the criminality rate for men and a 41% reduction in women." Also, **The reduction in criminality ranged from between 17%-46%.**
- Stimulants have a faster response time and often larger effect size than other medications.
- When evaluated over several weeks Strattera shows similar effect sizes to stimulants.
- Adverse effects are reported but typically are "non-serious" like insomnia and appetite suppression


 119

Medication Treatment of ADHD in children, Stimulant treatment shown to reduce core ADHD symptoms.

- Effect sizes have been moderate on **teacher ADHD rating scales for methylphenidate**
 - (SMD -.77, n=1698) (Storebo, et al., 2015)
- Effect sizes have been moderate on **teacher ratings on general behavior for methylphenidate**
 - (SMD -.87, n=668) (Storebo, et al., 2015)
- Parent ratings indicated moderate improvements on quality of life**
 - (SMD 0.61, three trials, n=514). (Storebo, et al., 2015)
- Methylphenidate was associated with **increased risk of non-serious adverse events**
 - (1.29, 21 trials, n=3132) **insomnia, appetite suppression, etc.** (Storebo, et al., 2015)

Someki & Burns, 2009:

- "A total of 81 effect sizes were computed with the following 'unbiased effect sizes':
 - Total **.53**
 - .11 for physiological measures,**
 - .38 for psychological measures**
 - .56 for behavioral measures.**
- Note: Largest effect size on behavioral measures.** Other effects would be considered significant but small.


 120

Stimulants vs. Strattera

Strattera is a non-stimulant Rx treatment for ADHD.

Some studies have found similarity of effect size with stimulant Rx, but a longer period to impact.

- Busche & Savill, (2014) "Using minimum 6-week clinical trial criteria, atomoxetine may demonstrate similar efficacy to methylphenidate comparing reduction in core ADHD symptoms in meta-analysis, although the diversity of the data makes interpretation complex."
- Hanwella, et al., (2011) did not find a significant difference between methylphenidate (**Ritalin**, etc.) and atomoxetine (**Strattera**). They concluded atomoxetine and methylphenidate had comparable efficacy and equal acceptability in treatment of ADHD in children and adolescents.
- Similarly, Hazell, et al., (2011) also conducted a meta analysis and found that **after 6 weeks 53.6 of atomoxetine and 54.4% of methylphenidate responded.** Again, arguing for "non-inferiority" of atomoxetine.

 121

Vyvanse is one of the newer drugs which has compared favorably to other Rx, at least on symptom reduction.

(Stuhec, et al., 2015)

28 trials were included in the meta-analysis.

Vyvanse was found to have a larger effect size than competitors in a few studies.

Efficacy in reducing ADHD symptoms compared to placebo:

bupropion (Wellbutrin , etc.)	(SMD=-0.32, 95% CI: -0.69, 0.05),
Atomoxetine (Strattera)	(SMD=-0.68, 95% CI: -0.76, -0.59)
methylphenidate (Ritalin , etc.)	(SMD=-0.75, 95% CI: -0.98, -0.52)
high efficacy lisdexamfetamine (Vyvanse)	(SMD=-1.28, 95% CI: -1.84, -0.71).

(Stuhec, et al., 2015)

Similarly Roskell, et al. (2014) found that Vyvanse (lisdexamfetamine) outperformed methylphenidate (**Ritalin**, etc.) (MPH), atomoxetine (**Strattera**) (ATX), and dexamfetamine (**Dexedrine**)(DEX) by an effect size of .51 to .82.



Medication Treatment of ADHD in children: Concerns 1.

An Old intervention: Medication Tx of ADHD has been around since the 1970's. Some progress, but...

Two common non-serious adverse events are insomnia and appetite suppression (Shaw, 2016). Less common: cardiac & suicidal events.

"Medication possession ratio" not taking the ADHD medication:
...a measure of how frequently ADHD patients take their Rx based upon prescription refills is below .7, so **"drug adherence and persistence are generally poor among patients with ADHD"**. (Gairia, et al., 2014).

Rx impact upon memory is more limited:
Executive memory (SMD) .26, 95% confidence interval .13-.39 (Coghill, et al., 2014).
Smith and Farah (2010) reported mixed results.
Are stimulants truly neurocognitive enhancers? (Weyandt, et al., 2016)

Prescription stimulants as a whole have not shown a statistically significant impact upon:
Attention (Repantis, et al., 2010)
Executive functioning (Weyandt et al., 2016)
Only a small number of studies which address examine these issues.



Medication Treatment of ADHD in children: Concerns 2.

Academic impact?
ADHD medications have shown limited **impact upon academic functioning** (Molina, et al., 2009).

Most meta-analyses of Rx for ADHD do NOT evaluate academic impact (Maneeton, et al., 2015; Shaw, 2016; Storebo, et al., 2015; Stuhec, et al., 2015; Coghill, et al., 2014)

Stimulant misuse by college students is a real concern.
Chen et al., 2016 report misuse of stimulants among the general population has risen by about 67% and ER visits rose by 156% from 2006 to 2011.
DeSantis, Webb, & Noar, 2008 found prevalence rates as high as 43%.
Benson et al., 2015 reported an average of 17% misuse.


Costs:
"...behavior modification (large-group parent training) was less costly for a school year of treatment (**\$961**) than beginning treatment with a low dose of stimulant medication (**\$1,669**), regardless of whether the initial treatment was intensified with a higher "dose" or if the other modality was added (Page, et al., 2016). These are notable expenses.



Elaboration:
Prescription Stimulant Misuse in college students
 (Weyandt, et al., 2016)


Factors related to higher rates of medication misuse: Males, Caucasians, those who have higher rates of membership with sororities and fraternities, students with lower grades, who procrastinate more, struggle with time management, and who have higher rates of risky behavior and more substance abuse.

Symptoms predictive of prescription stimulant misuse: inattention, depression, anxiety, stress, internal impulsivity and internal restlessness & higher misuse rates among those "who had at some point been prescribed stimulant medication to treat ADHD."

 125

Elaboration: Some benefits of medication on areas of cognitive functioning, but relatively limited.

- Rx impact upon memory is more limited, **executive memory (SMD) .26**, 95% confidence interval .13-.39 (Coghill, et al., 2014).
- "Forty-three studies involving a pooled total of 2,110 participants were identified for inclusion. **Drug treatment benefited children in the amount of school work that they completed, by up to 15 %, and less consistently improved children's accuracy** in specific types of academic assignments, such as arithmetic. Similar **improvements were seen in classroom behaviour, with up to 14 % more of children's time spent "on task".**" (Prasad, et al., 2013).

 126

Behavioral Tx of ADHD in children, *highlights* of positive findings.


•7 meta-analyses found (Not Exhaustive). Main outcome measure mean improvement on ADHD rating scale compared with control conditions.

•**Preschoolers:** Parent training resulted in improved parenting and moderate improvement upon ADHD rating scales (Mulqueen, et al., 2015).

School-aged Parenting improvements: "With probably blinded assessments, significant effects persisted for **parenting** (SMD for positive parenting 0.63; SMD for negative parenting 0.43) and **conduct problems** (SMD 0.31)." (Daley, et al., 2014).

Behavior mean effect sizes were positive and significant: "for within-subjects (0.72) and single-subject (2.20) designs, but not for between-subjects (0.18) designs." However, the between-subjects design is a small effect size (DuPaul, et al., 2012). "...moderate effect size at post-treatment that decreased to a small effect size at follow-up." (Lee, et al., 2012)


"**Parenting competence was the only outcome that had a large effect, which decreased to moderate at follow-up. The strength of the effect differed between questionnaire and observation measures.**" (Lee, et al., 2012)

 127

Behavioral Interventions:
Meta-analysis 1: Intervening with parents of preschoolers.
 (Mulqueen, et al., 2015).

Moderate **improvement on ADHD rating scales** (SMD=.61) compared with controls. Suggesting parent interventions for preschoolers with ADHD are efficacious (Mulqueen, et al., 2015).

Welcome news for parents of preschoolers with ADHD as many are very uncomfortable with medicating such young children.



128

Behavioral Interventions Meta-analyses 2: Effects of school-based interventions for ADHD: A meta-analysis 1996-2010.
 (DuPaul, et al., 2012)


60 studies examined.

Behavior mean effect sizes were positive and significant: "for within-subjects (0.72) and single-subject (2.20) designs, but not for between-subjects (0.18) designs." However, the between-subjects design is a small effect size.

Academic findings, again, less persuasive:

Mean effect sizes for academic outcomes were positive but **not significant** for between-subjects (0.43) and within-subjects (0.42) design studies, but were **positive and significant only for single-subject** (3.48) design studies.

The mixed academic effects raises doubts about the academic gains. Only positive outcomes for academics were only found for single-subject design studies calls into question how robust such findings actually are.




129

Behavioral interventions with ADHD:
 Meta-analysis of RCT's
 (Daley, et al., 2014)

"Thirty-two of 2,057 non-duplicate screened records were analyzed. For assessments made by individuals closest to the treatment setting (**usually un-blinded**), there were significant improvements in **parenting** quality (standardized mean difference [SMD] for **positive parenting** 0.68; SMD for **negative parenting** 0.57), **parenting self-concept** (SMD 0.37), and **child ADHD** (SMD 0.35), **conduct problems** (SMD 0.26), **social skills** (SMD 0.47), and **academic performance** (SMD 0.28)."

"With **probably blinded assessments**, significant effects persisted for **parenting** (SMD for positive parenting 0.63; SMD for negative parenting 0.43) and **conduct problems** (SMD 0.31)."

Their Conclusion: There is blinded evidence that parenting is improved and there is a decrease in conduct problems.




130

Behavioral interventions with ADHD:
Meta-analysis of RCT's
(Daley, et al., 2014)

Since this is one of the rare meta-analyses of behavior interventions of ADHD that included consideration of academics is worth consideration.

Academic performance: Only was with un-blinded raters (individuals closest to the treatment setting) was there a significant, but small effect: (SMD .28). With un-blinded raters there was no significant effect upon academics.



131

Meta-analysis of behavioral parent training (BPT) with ADHD children
(Lee, et al., 2012)


40 studies included. Outcomes were focused upon child behavior, parent behavior, and parental perception of parenting. No academic outcome measures were reported.

“The majority of outcome categories were associated with a moderate effect size at post-treatment that decreased to a small effect size at follow-up.”

“Parenting competence was the only outcome that had a large effect, which decreased to moderate at follow-up. The strength of the effect differed between questionnaire and observation measures.”

Interesting, not surprisingly, sustainability concern: “Difficulty with sustaining changes over time was noted for both parent and child behavior. The effect of BPT dissipated rapidly when the behavioral contingencies were terminated, which was more likely to happen when assistance provided by the group or the therapist ended at follow-up (Hinshaw, 2009). Follow-up sessions of BPT may be necessary to address continuous use of the contingency techniques at home.”

Noteworthy: Negative correlation was found between comorbid ODD or other behavioral problems and the ES of this intervention.



132

A meta-analysis of behavioral treatments for ADHD.
(Fabiano, et al., 2009)


“One-hundred seventy-four studies of behavioral treatment were identified from 114 individual papers that were appropriate for the meta-analysis.”

ADHD parent ratings, teacher ratings with only between 3-5 studies focused upon observed behaviors. ES for parent and teacher ratings were in the moderate range. Observations ES were slightly lower.

“Overall unweighted effect sizes in between **group studies (.83)**, pre-post studies (.70), within group studies (2.64), and single subject studies (3.78) indicated that behavioral treatments are highly effective. Based on these results, there is strong and consistent evidence that behavioral treatments are effective for treating ADHD.”

No conclusions are made regarding academic functioning.

NOTE: Arguably between group studies would be considered to have the most empirical weight of the number of different designs reported above.



133


Behavioral Interventions Meta-analyses 3: Learning and delayed memory in children with ADHD: A meta-analytic review 2014.
(Kolomeyer, et al., 2014)

Well-documented learning deficits persist despite pharmacological treatment and intensive behavioral interventions (Molina et al., 2009). *It remains unclear why cohorts with ADHD continue to experience marked academic difficulties.* *Maybe there are memory deficits?*

“The current study is a comprehensive meta-analysis of 38 studies **conducting delayed memory trials** with ADHD children and their typically developing peers. “

“**An analysis of 20 of the 38 studies has been completed to date.** Complete data entry and statistical analyses will be completed by March 2014. **The preliminary analysis revealed that children with ADHD exhibited moderate magnitude impairments on delayed memory tests (g = 0.658, 95% CI = 0.314 to 1.003).** Significant heterogeneity among the studies supports the analysis of potential moderators (Q = 156.70, df = 19, p < .0001).”

So, memory is a deficit for ADHD children.



134

Behavioral Tx of ADHD in children, *highlights* of concerns.

•7 meta-analyses found (Not Exhaustive).

Reliance on rating scales. **Lack of studies with objective measures of behavior.**

No claims can be made about cognitive functioning: not measured.


Sustainability of effects a concern once therapy is over.

Negative correlation with comorbid ODD or other behavioral problems reducing effect size.

No substantial claims can be made about academics as it was not studied or there was a lack of effects.

Children with ADHD show substantial deficits in delayed memory, attention and working memory and academic struggles which are issues not addressed with this modality.

Costs? Vary, but as previously noted somewhat less than medication treatment for a year. (Page, et al., 2016).



135


Consider the MTA (Multi-Modal Treatment of ADHD) at 6 and 8 year follow-up in which both Rx and Behavioral Tx used.
(Molina et al., 2009)

Considered by many to be the best ADHD intervention study ever conduct with the best interventions available at the time. Randomly assigned 14-month treatments in the NIMH Collaborative Multisite Multimodal Treatment Study of Children With Attention-Deficit/Hyperactivity Disorder (MTA; N = 436);

It captures the limits of traditional approaches.

At 6 and 8 years follow up of a 14 month intensive treatment program the ADHD children in 4 distinct treatment groups had fared worse than a comparison group on 91% of the variables considered (Molina, et al., 2009). Those variables included grades earned in school, arrests and other clinically relevant outcomes.

Why does this time frame matter?
Many children with ADHD get diagnosed at age 7.
They will be close to graduation at about 17, or NOT.



136

Rx may reduce core ADHD symptoms but. There is much it doesn't address. Consider MTA:
(Molina et al., 2009)

What were the original 4 treatment groups? Best medication regimen developed to date
 Extensive behavioral management
 Combination of both
 Typical psychiatric community care.

It is instructive to look for this study online and see how extensive the treatment actually was.


While follow-ups at 2 and 4 years appeared positive. At 6 and 8 years not so much...

At 6 and 8 years the 4 intervention groups were indistinguishable.

Symptom trajectory through 3 years predicted outcome in subsequent years compared to non-ADHD peers (local normative comparison group; *N* = 261).

SYMPTOM TRAJECTORY IS A WAY TO CONSIDER "SEVERITY".

MTA participants fared worse than the local normative comparison group on 91 % of the variables tested.


1

Disappointing results for long term Tx outcome.
(Molina, et al., 2009)


***Medication use decreased by 62% after the 14-month controlled trial, but adjusting for this did not change the results.** ADHD symptom trajectory in the first 3 years predicted 55% of the outcomes. **This is the issue of poor drug adherence and persistence noted previously.**

Conclusions: Type or intensity of 14 months of treatment for ADHD in childhood (at age 7.0-9.9 years) does not predict functioning 6 to 8 years later.

Thus children with behavioral and socio demographic advantage, with the best response to any treatment, will have the best long-term prognosis.

***As a group, however, despite initial symptom improvement during treatment that is largely maintained after treatment, children with combined-type ADHD exhibit significant impairment in adolescence.**

Authors stated: **"Innovative treatment approaches targeting specific areas of adolescent impairment are needed."**



1

The data so far suggests benefits and limits of traditional approaches to ADHD treatment.

The MTA study results suggest that the children in their study with combined type ADHD also need targeted innovations.

I would argue that in my direct experience with clients and family members, that with milder ADHD-I, even with no comorbidity that they often need both medication and behavioral interventions at least at some time over their development **AND** they need more to accomplish academic and occupational success.

Hence innovations should be take seriously...


119

Working memory training & ADHD
Meta analyses: Positive findings.

4 relevant meta-analyses were found. By the way now there are over 100 peer reviewed published studies specifically on Cogmed – all since 2002.

WM training resulted in "short-term improvements in **verbal WM, visuo-spatial WM, and word decoding** in children with LDs after training (**effect sizes ranged between 0.36 and 0.63**), when compared to the untrained control group. **These improvements sustained over time for up to eight months.** Furthermore, children > 10 years seemed to benefit more in terms of verbal WM than younger children, both immediately after training as well as in the long-term." (Peijnenborgh, et al., 2016)

According to the meta analysis of Cortese, et al., (2015): "There were significant effects on laboratory tests of **working memory (verbal: SMD = 0.52, 95% CI = 0.24-0.80; visual: SMD = 0.47, 95% CI = 0.23-0.70)** and **parent ratings of executive function (SMD = 0.35, 95% CI = 0.08-0.61).**"

"Meta-analyses indicated that the programs produced **reliable short-term improvements in working memory skills.** For verbal working memory, these near-transfer effects were not sustained at follow-up, whereas for **visuospatial working memory, limited evidence suggested that such effects might be maintained.**" (Melby-Lervag & Hulme, 2013).



Efficacy of working memory training in children and adolescents with learning disabilities: A review study and meta-analysis
(Peijnenborgh, et al., 2016)

NOTE: While the title suggests a focus on LD the authors state within the article that "Almost all the studies included children with ADHD." (p. 7).

"The meta-analysis indicated reliable short-term improvements in **verbal WM, visuo-spatial WM, and word decoding** in children with LDs after training (**effect sizes ranged between 0.36 and 0.63**), when compared to the untrained control group. **These improvements sustained over time for up to eight months.** Furthermore, children > 10 years seemed to benefit more in terms of verbal WM than younger children, both immediately after training as well as in the long-term." (Peijnenborgh, et al., 2016)



Cognitive training for ADHD: Meta-analysis of clinical and neuropsychological outcomes from RCT's
(Cortese, et al., 2015)

"The authors performed meta-analyses of randomized controlled trials to examine the effects of cognitive training on attention-deficit/hyperactivity disorder (ADHD) symptoms, neuropsychological deficits, and academic skills in children/adolescents with ADHD."

"Sixteen of 695 nonduplicate records were analyzed (759 children with ADHD)."

"There were **significant effects on laboratory tests of working memory (verbal: SMD = 0.52, 95% CI = 0.24-0.80; visual: SMD = 0.47, 95% CI = 0.23-0.70)** and **parent ratings of executive function (SMD = 0.35, 95% CI = 0.08-0.61).** Effects on academic performance were not statistically significant. There were no effects of working memory training, specifically on ADHD symptoms."




Do programs that train working memory, other executive functions, and attention benefit children with ADHD? A meta-analytic review of cognitive, academic and behavioral outcomes.
(Rapport, et al., 2013)

25 studies reviewed. "Random effects models corrected for publication bias and sampling error revealed that studies training short-term memory" **showed improvements in short-term memory of a moderate magnitude ($d = 0.63$).**

"Far transfer effects of cognitive training on academic functioning, **blinded ratings of behavior (both non-significant), and cognitive tests ($d = 0.14$) were nonsignificant or negligible.**"

"Unblinded raters ($d = 0.48$) reported significantly larger benefits relative to blinded raters and objective tests (both $p < .05$),"

 143

Is working memory training effective? A meta-analytic review.
(Melby-Lervag & Hulme, 2013)

23 studies with 30 group comparisons were made.


"Meta-analyses indicated that the programs produced reliable short-term improvements in working memory skills. For verbal working memory, these near-transfer effects were not sustained at follow-up, whereas for visuospatial working memory, limited evidence suggested that such effects might be maintained."

These authors question the usefulness of such training without finding more generalization to other skills.

The authors acknowledge that memory training produces "short-term, specific training effects that do not generalize." Is this really about 'transfer' not generalization? The subjects were measured on objective measures of the constructs different than the activities done in the training.


They do acknowledge: "Possible limitations of the review (including age differences in the samples and the **variety of different clinical conditions included**) are noted." **This is no small consideration.** As has been well established previously today: severity & comorbidity are rather substantial considerations in all interventions. Which these authors ignore.

One question becomes does such training have clinical relevance?

 144

Are WM deficits clinically relevant for those with ADHD?
Does some other intervention address them more effectively?

1. Academic achievement highly correlated to WM capacity.
2. Employment strongly related to academic achievement (e.g. high school grad. Vs. college).
3. ADHD: Lower high school and college graduation rates.
4. ADHD: Unemployed and underemployed at lower rates.
5. Higher inattention levels are more strongly correlated with lower levels of employment.
6. Rx no notable impact upon academic functioning, working memory, etc.
7. Behavioral interventions have not been shown to improve WM.
8. Kasper et al., (2012) found that children with ADHD showed significant and "large magnitude working memory deficits" in both verbal and visual spatial WM compared to typical developing peers. Martinussen et al., (2005) found such deficits to be of ES levels of **.85 spatial storage, 1.06 spatial central executive WM, .47 verbal storage, .43 verbal central executive WM.**
9. Alderson et al., (2013) found that adults with ADHD continued to have moderately sized deficits in verbal WM, visual spatial WM & central executive WM.

 145

Working memory training for children with ADHD , *highlights of concerns 1*

Reduction of the core ADHD symptoms based upon meta-analyses have not been found. (Although it has been found in some individual studies.) It is possible more research may find this. It is also possible it won't.

WM training has not been shown to accomplish far transfer to academic gains in the context of a meta-analyses. (Although it has been found in some individual studies – a number of those are Cogmed studies.) Since there is a strong relationship between WM and academic gains there is some expectation that this will develop over time. It is possible more research will find this. It is also possible it won't.

Another consideration is that direct academic remediation may be necessary to achieve far transfer after WM training. The issue is whether far transfer then occurs? Or without WM training are children with WM deficits likely to be successful with direct remediation ?

IMPORTANT CAUTIONS: It is noteworthy that neither medication treatment of ADHD nor behavioral treatment of ADHD have been found to show far transfer to academic gains at least in meta-analyses. However, given that both of those interventions have been around for several decades one might argue it would be more likely it would have been found by now.



Working memory training for children with ADHD , *highlights of concerns 2*

Costs? Previously some have argued this intervention is expensive. One issue is that traditional interventions are often covered by insurance while this intervention typically is not, but that is not true in all countries. In terms of face value the expense of this intervention is no longer much different than traditional alternatives. However, the length of time it has been found to last notably exceeds that of traditional interventions.



It appears unlikely that any one approach alone will be enough.

If the goal is to impact the developmental trajectory of children with ADHD so as to increase academic and occupational success then one type of intervention is unlikely to get that done.

- Is it enough to reduce core ADHD symptoms?
- Is it enough to reduce conduct disorder or oppositional defiant disorder?
- Is it enough to improve social skills?
- Is it enough to improve working memory?

To impact their developmental trajectory these children need more far transfer from the combination of all of the interventions to improved academic & occupational success.

We think this requires collaborative efforts across these various methods of intervention.

This is especially true for the more severe cases, who are also more likely to persist with ADHD into adulthood.

Severity and comorbidity are variables which have been ignored in all of these meta-analyses. We believe that is an clinical and empirical error. The following slides discuss this issue related to Cogmed.




Combining Rx with Cogmed: Improved behavior & Cognitive functioning.

Are such combinations more reasonable than solo interventions?

That depends upon the goal of treatment.

Additionally, in our slide which highlighted in red font those studies which have resulted in far transfer to academic gains, but a new study provides a new framework for the likelihood of far transfer related to, but distinct from severity, co-morbidity and whether a patient is taking Rx: **temperament, more specifically "effortful control"**.



WM training in children: Effectiveness depends on temperament: "Effortful control"


(Studer-Luethi, Bauer & Perrig, 2016)

This was NOT a Cogmed study, but it was a study of another form of WM training – n-back training. Considered the temperament factors of "effortful control" and neuroticism.

N=99, second graders randomly assigned to WM training for 20 sessions, computer-based reading training or a no-contact control group.

They did find near transfer to VSWM, far transfer to a vocabulary task, and increased academic achievement in reading and math by trend.

However, the temperament variable "effortful control" predicted larger training mean and gain scores and that there was a moderation effect of both temperament factors on post-training improvement: WM training condition predicted higher post-training gains compared to both control **conditions only in children with high effortful control or low neuroticism**. Our results suggest that a short but intensive WM training program can enhance cognitive abilities in children, but that **efficient self-regulative abilities and emotional stability are necessary for WM training to be effective.**" Effortful control...




"Effortful Control": In many ways the opposite of hyperactivity, impulsivity, externalizing, etc.

Studer-Luethi, Bauer & Perrig, (2016) capture "effortful control" in this way:

'One predisposition for self-regulation skills is the temperament factor called effortful control (Rothbart & Bates, 2006). It is believed to be associated with early-appearing individual differences in self-regulation, and with it the developmental process underlying conscientiousness (Ahadi & Rothbart, 1994). It allows individuals to voluntarily regulate their behavior in relation to current and future needs, as for instance to inhibit a dominant response in favor of a subdominant response (Blair & Diamond, 2008; Derryberry, Reed, & Pilkenton-Taylor, 2003).'

"...Effortful control overlaps substantially with inhibitory control (see Diamond, 2013), but while executive functions emerge from a neural system approach with a historical focus on volitional control of cognitive self-regulation, **effortful control historically focused more tightly on automatic or nonconscious emotional regulation** (cf. Blair & Razza, 2007; see also Eisenberg, Spinrad, & Eggum, 2010; Mischel & Ayduk, 2002)." (My underlining, bold and italics added.)

Or effortful control is the opposite of hyperactivity, impulsivity, externalizing, aggression, etc.



Effortful Control: A key consideration in the transfer of Cogmed Effects.

(Osa, et al., 2014)

	Effortful Control
SDQ – parents ADHD	-.41
SDQ-parents Externalizing problems	-.39
SDQ-parents Total	-.35
SDQ-Teachers ADHD	-.30

Pearson Correlations and internal consistency of measures.

Table of variables inversely related to Effortful control

Data supports this posed 'inverse correlation'.

SDQ: Strengths and Difficulties Questionnaire for 3 and 4 year olds.

As is seen here elevated ratings of ADHD or externalizing behaviors are inversely related to "effortful control".

Pearson 1

Factor Loadings for CBQ models

(Osa, et al., 2014)

	Effortful Control
Activity level	-.448
Anger/frustration	-.222

A couple interesting factor Loadings.

Other variables inversely related to Effortful control

This rather interesting data further supports this posed 'inverse correlation'.

This temperamental factor of "effortful control" gives another way to understand why some more substantially benefit from Cogmed than others.

This adds further understanding of how to facilitate far transfer with Cogmed.

Pearson 1

Multiple treatments & consideration of severity of disorder and comorbidity: The wave of the future?

A more refined approach has been recently assumed by some WM training researchers. That is to consider severity and comorbidity. This was considered in our recent webinar: "Differentiating Cogmed Effects: ADHD, LD and WM deficits." Roording-Ragetie, et al., (2016) and Van der Donk, et al., (2016) conducted two Cogmed-specific studies with this approach of differentiating between groups. Their results support the logic of this approach. That is severity and comorbidity did affect far transfer.

Multiple treatments may be the way to holistically impact upon ADHD patients.


With some new research a different consideration, temperament and/or 'effortful control' can be considered. Intriguingly a Cogmed-specific study by Foy & Mann (2014) found that "executive control" & WM were improved when low income minority kindergartners did Cogmed.

On a clinical and educational level we suggest to consider the trajectory of the individual child with ADHD to determine what makes sense for that child which and in what order interventions should be delivered to constructively impact his or her developmental trajectory.

Pearson 19

Summary

- Working Memory, among those with ADHD, tends to develop minimally whereas it increases substantially for typically developing children. Working memory is strongly correlated with academic achievement.
- ADHD children are at risk for numerous academic, social, behavioral, occupational and law enforcement concerns.
- ADHD-C is a more severe disorder than ADHD-I. Severity and co-morbidity can limit or interfere with the impact of any intervention.
- ADHD-I students tend to have more problems with academic problems than ADHD-C students. More girls, teens & adults have ADHD-I than ADHD-C. Inattention tends to persist into adulthood whereas hyperactivity/impulsivity tends to wane.
- Medications have been found to be quite effective in improving the core symptoms of ADHD based upon parent and teacher ratings. Little evidence for objectively measured cognitive functions such as attention, working memory, etc. Rather limited evidence for academic improvement.
- Behavioral interventions for parents of preschoolers have been found to have significant small to moderately sized effects in improved parenting, reducing conduct problems, improving some behavior related to ADHD. Concerns about sustainability of these interventions when therapist involvement ceases persist. No evidence for objectively measured cognitive functions such as attention, working memory, etc. No evidence for academic gains.
- WM training has been found to significantly improve verbal working memory and visual spatial working memory which has been sustained up to 8 months.
- Multiple therapies is the more plausible route to helping more children with ADHD.
- Severity and comorbidity are ignored in meta-analyses. This is an oversight and confounds the results from such approaches.
- Temperament or "effortful control" is a factor to consider in evaluating the likelihood of far transfer and/or facilitating far transfer.

 158

Presenter: Charles Shinaver, Ph.D.
Cognitive Consultant
(888) 748-3828, x110
(800)627-7271 x 262355
(317) 641-7794
charles.shinaver@Pearson.com

Presenter:
Peter Entwistle, PhD
Cognitive Consultant
888-748-3828, x111
202-333-3210
Peter.entwistle@pearson.com

  1
