

What does Cogmed tell us about brain functioning?
 A review of recent research



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Prevailing wisdom? Or Dogma?
Scientific dogma until 1970' s...

“In the adult [brain] centres, the nerve paths are something fixed, ended, immutable. Everything may die, nothing may be regenerated.”

Santiago Ramon v Cajal (1913). Spanish physician, neuroanatomist & Nobel Laureate



So, does WM training (Cogmed) **enhance** WM capacity?

Is working memory capacity a malleable factor?
Can it be improved by computerized training?

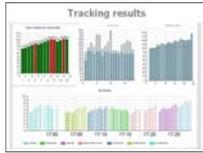
By improving a person's WM, beneficial effects should also be expected in various related abilities utilizing WM, including real-world behavior (beyond the Laboratory)

Features of Cogmed WM Training

- ▶ Intensive & adaptive training
 - *Adaptive*: automatically, continuously adjusted in difficulty relative to individual's WM capacity
 - *Extensive repetition, practice, feedback* – designed to enhance the development & efficiency of underlying neural substrates (for WM)
 - *Underlying assumption*: improvements in WM will generalize or transfer to other tasks or activities that rely on the same neural networks or require WM (Klingberg, 2010)

Computerized Working Memory Training (Cogmed JM/RM/QM)

- ▶ 45 min training/day
- ▶ 5 days/week, 5 weeks
- ▶ Adaptive algorithm
 - individually-based
- ▶ Reinforcement
 - Immediate performance-based feedback;
 - internal reinforcement activities
 - external reinforcement for completing pre-specified # sessions
- ▶ Weekly monitoring calls from licensed provider, using uploaded tracking data



Cogmed/Pearson
<http://www.cogmed.com/rm>

What does the training entail?

- ▶ EQUIPMENT
 - Software (license per person)
 - Computer (per person) linked to internet
 - [Headphones for group administration]
- ▶ COACHING/Supervision
 - *Weekly telephone call* from a trained & licensed 'coach' to give feedback on performance, give advice about training activities, answer questions
 - *For youth - Daily supervision of training* - parent, school-aide, volunteer, (often by members of research study)

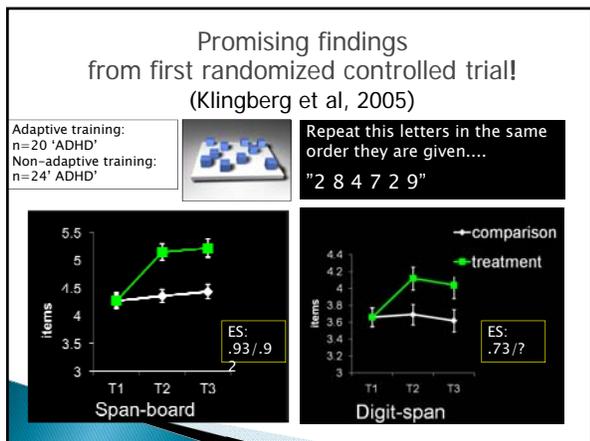
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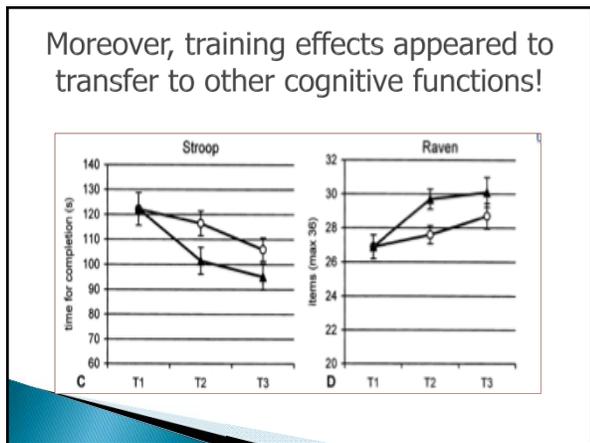
The beginning...a startling finding suggesting that WM might be mutable – like a muscle!

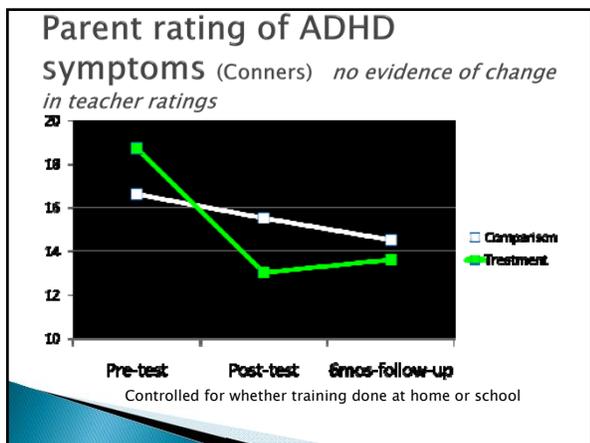
But a very small sample (n ~ 7 per group)
 Double-blind but not randomized



- ▶ In 2002, Torkel Klingberg, a Swedish researcher challenged the prevailing notion that WM capacity is fixed - he reported that 5 weeks of playing specific memory-based computer games (every day for about 30-45 mins), not only boosted WM, of children with ADHD but also intellectual ability!





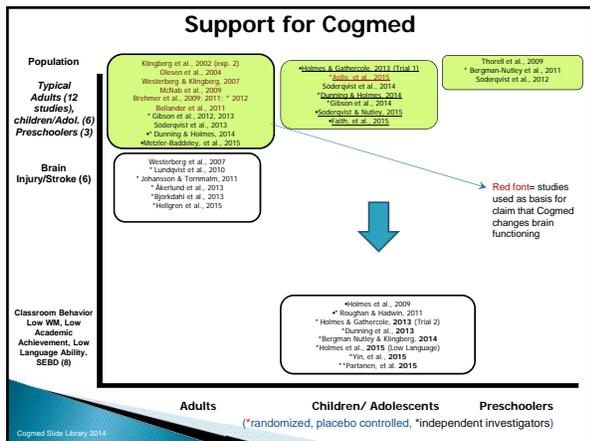


The spread of Cogmed

~76 published studies; 90+ ongoing studies

- *Healthy young adults*
- *Older/elderly adults*
- *Adults who have had a stroke*
- *Individuals with brain injury*
- *Children with: WM deficits; **ADHD**; cochlear implants; cancer treated with radiation; Down syndrome, low IQ, born prematurely...*

Cogmed is now operating in > 1000 schools world-wide (& is available in NZ)

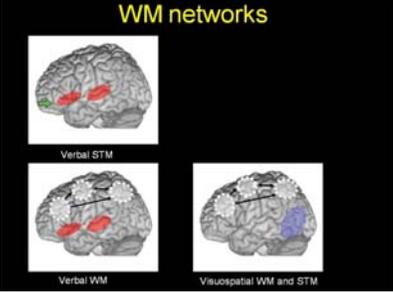


Evidence?

▶ Is there any scientific evidence that the brain actually changes as a result of Cogmed?

Curtis & D'Esposito

WM networks



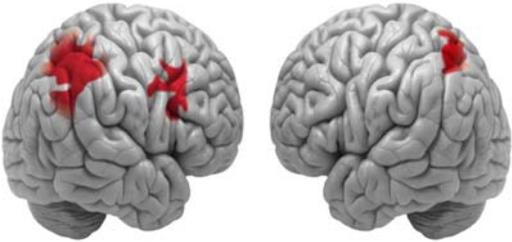
Verbal STM

Verbal WM

Visuospatial WM and STM

This slide shows three brain maps illustrating working memory (WM) networks. The top map is labeled 'Verbal STM' and shows red activation in the left inferior frontal gyrus. The bottom-left map is labeled 'Verbal WM' and shows red activation in the left inferior frontal gyrus and the left superior parietal lobule. The bottom-right map is labeled 'Visuospatial WM and STM' and shows red activation in the left superior parietal lobule and blue activation in the left inferior frontal gyrus.

Olesen et al 2004



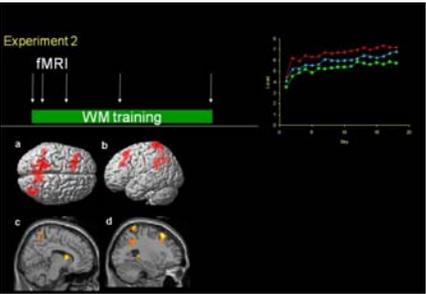
This slide displays two lateral views of a human brain. Red activation is visible in the left superior parietal lobule on both views, indicating the location of the visuospatial working memory network.

Olesen et al 2004

Experiment 2

fMRI

WM training



a b

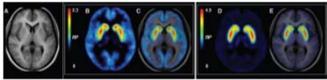
c d

This slide presents fMRI results for Experiment 2. At the top, a diagram shows 'fMRI' scans occurring during 'WM training'. Below this, a line graph plots BOLD signal change over time, showing an increase in signal during training. Four brain maps (a, b, c, d) show activation in the left superior parietal lobule. Maps a and b are lateral views, while c and d are axial views.

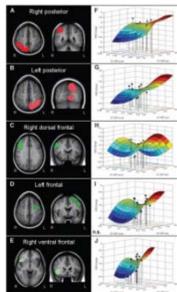
Source

- ▶ *Science* **323**, 800 (2009);
 - ▶ Fiona McNab, *et al.*
- ▶ Changes in Cortical Dopamine D1 Receptor Binding Associated with Cognitive Training

MRI studies of the Human Brain



Brain Locations



Working memory plasticity modulated by dopamine transporter genotype
Yvonne Brehmer, Helena Westerberg, Martin Bellander, Daniel Fürth, Sari Karlsson, Lars Bäckman (2009)

- ▶ Dopamine (DA) is implicated in working memory (WM) functioning. Variations in the DA transporter (DAT1) gene (SLC6A3) regulate DA availability in striatum.
- ▶ Compared to DAT1 9/10-repeat carriers, homozygosity of the DAT1 10-repeat allele has been related to less active dopaminergic pathways.
- ▶ A group of younger adults received 4 weeks of computerized adaptive training on several WM tasks.

WM Plasticity

- ▶ All participants improved their performance as a function of training. However, DAT1 9/10-repeat carriers showed larger training-related gains than DAT1 10-repeat carriers in visuo-spatial WM. By contrast, the two groups were indistinguishable in baseline WM performance as well as in a variety of tasks assessing different cognitive abilities. This pattern of results provides novel evidence that WM plasticity is a more sensitive indicator of DAT1 gene-related cognitive differences than single-assessment performance scores.

Dopamine, Working Memory, and Training Induced Plasticity: Implications for Developmental Research

- ▶ Söderqvist, S., Bergman Nutley, S., Peyrard-Janvid, M., Matsson, H., Humphreys, K., Kere, J., & Klingberg, T. (2011, November 21). Dopamine, Working Memory, and Training Induced Plasticity: Implications for Developmental Research. *Developmental Psychology. Advance*
- ▶ online publication. doi: 10.1037/a0026179

Dopamine & Working Memory?

- ▶ This article reviews some of the evidence for the role of dopamine in WM functioning, in particular concerning the link to WM development and cognitive plasticity. Novel data are presented showing that variation in the dopamine transporter gene (*DAT1*) influences improvements in WM and fluid intelligence in preschool-age children following cognitive
- ▶ training. Our results emphasize the importance of the role of dopamine in determining cognitive
- ▶ plasticity.

Where are we today?

- ▶ Is there anything new?

NEW Cogmed Research:
Cognitive Training Enhances
Brain Connectivity in Childhood
(Astle, et al., 2015)



Cogmed's Impact upon the Brain Neurophysiology in Children (*Typically Developing*) (Astle, et al., 2015)

This study considered the Neural Basis for Cogmed Training Effects in a systematic, controlled manner in children.

Typically developing children.
 n=33, 6 did not finish training leaving n=27.
 Children between 8 to 11 years old.
 13 adaptive group (3 boys), 14 in placebo group (7 boys)
 Average age adaptive=119.2 months. (9.93 years)
 Average age non-adaptive=118.8 months (9.9 years)
 Groups were not significantly different based upon gender or age.

Exclusion Criteria: Developmental Disorder Diagnosis or an acquired neurological condition.

Design: Double Blind, Randomized, Placebo-Controlled Trial (**non-adaptive Cogmed**). **RCT.**

Treatment group did Cogmed RM.
 Control did non-adaptive Cogmed.



Cogmed's Impact upon the Brain Neurophysiology in Children (*Typically Developing*) (Astle, et al., 2015)

- ▶ **Cognitive Assessments:** Pre/Post Training: AWMA Automated Working Memory Assessment: Verbal Short Term memory (VSTM), Spatial Short Term Memory (SSTM), Verbal Working Memory (VWM), Visual Spatial Working Memory (VSWM). No pre-training differences.
- ▶ **MEG: Magnetoencephalograph (MEG):** Pre/Post Training. Data acquisition and basic preprocessing is outlined in detail in the study. Same process used pre/post. A high-density whole-head Vector View MEG system (Elekta-Neuromag) containing a magnetometer and two orthogonal planar gradiometers at 102 positions (306 sensors in total). See article for other details.
- ▶ **Training:** Cogmed training at home. Progress monitored remotely by research team. Children completed a minimum of 20 sessions of training with an upper limit of 25 training sessions.
- ▶ **Adaptive training:** Treatment group.
- ▶ **Non-Adaptive training:** Control group.

Cogmed's Impact upon the Brain Neurophysiology in Children (*Typically Developing*)

Post Cogmed Training: Among typically developing children connectivity between fronto-parietal networks and both lateral occipital complex and inferior temporal cortex was altered in a way that mirrored improvements in WM capacity. *In other words the increase of connectivity correlated with the magnitude of improvement in WM capacity. This change was greater in those that completed adaptive Cogmed than non-adaptive.*

This was based upon using a relatively new technique: MEG – Magnetoencephalography.



How new?
 My neuro-radiologist/wife saw it and said:
 "What is that?!" I've never seen that before."

Pre/Post Magnetoencephalograph Data

- ▶ Magnetoencephalograph (magnetic brain writing). A measure of the magnetic fields of the brain which indicates neuronal activity.
- "Magnetoencephalography (MEG) is a non-invasive neurophysiological technique that measures the magnetic fields generated by neuronal activity of the brain (Figure 1)." (<http://web.mit.edu/kit/mitmeg/whatis.htm>).

▶ Here on youtube you can get a helpful explanation of MEG: <https://www.youtube.com/watch?v=X8AJI7-jKI4>

We will describe this approach in a pragmatic and rudimentary way.



Magnetoencephalograph

First Coils are attached to the head:

Then a number of measurements are taken at the nose, the ears, and then at all coils.



Finally, measurements are taken across the head back and forth with a wand. The shape of the head is measured.

Then the subject is put in a room with a MEG scanner. All metals are removed and the scan is conducted.

Magnetoencephalograph

▶ Here is a subject in a room with a magnetic scanner:

As can be seen this will be a resting state measurement of activity.



▶ A recording of brain activity is taken while techs can see the subject and talk to him through a intercom.

Magnetoencephalograph (MEG)

Quantum mechanics concepts of superconductivity and tunneling are used to explain how the MEG works but are beyond our scope for the present webinar. An explanation is given in this video: <https://www.youtube.com/watch?v=FR7SP9eNd0k> (1)

In this video, MEG was described in the following way:
MEG is the successor of EEG: Electro-Encephalograph:
"Electric brain writing." (1)

"EEG measures your brain waves. It is an old technique and has been around for a century. It has problems. To solve those problems people started to think if we could measure the brain's magnetic fields. They are tiny fields. That we can measure them is a phenomenal achievement." (1)

Advantages of MEG:

- ▶ "MEG is **faster** than fMRI and PET, as it measures brains' electromagnetic activity, rather than their fuel consumption."
- ▶ "MEG is **more precise** than EEG, as the signals MEG detects are less distorted (as a result of superconductivity and tunneling) by passing through the brain and skull tissue that gets in the way. The magnetic changes are a more direct measure of brain activity. MEG is **more accurate**."

<https://www.youtube.com/watch?v=FR7SP9eNd0k>



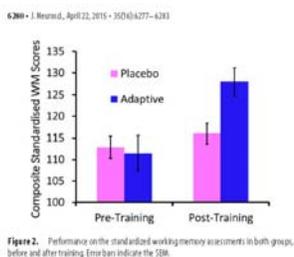
Key Aspects of Magnetoencephalograph - MEG

- ▶ For our purposes the key issues with MEG are:
 - The method involves measuring the electromagnetic activity of the brain. This is considered a more direct, accurate and precise measure of neuronal activity than EEG.
 - It is a way to measure brain activity **at rest**.
 - Effects seen while at rest cannot be attributed to strategy.
There is no strategy engagement while resting.
 - Effects seen while at rest cannot be attributed to motivation.
There is no need to be motivated while resting.

MEG rarely been used with children to evaluate the effects of training or therapy.

- An APA data-base search in 2015 of *magnetoencephalography & training & children* resulted in only 3 relevant articles (noted below).
- Same search was repeated with “therapy” replacing “training”. Still only the 3 articles below were relevant.
 - All of these studies were published since 2005.
- Only the search for “training” not “therapy” resulted in relevant articles:
 - *Exercise-induced neuroplasticity in congenital hemiparesis.*
 - Altering brain circuits for reading through intervention.
- One year music training on the effects of development of auditory cortical-evoked fields in young children.

Improvement in WM Capacity on the Group level of Adaptive vs. “Placebo”. (Aste, et al., 2015)



Critical Finding:
Cogmed’s Impact upon the Brain Neurophysiology in Children (Aste, et al., 2015)

- ▶ **Critical Finding:** “Improvements in WM (on untrained tasks) after training were associated with *increased strength of neural connectivity at rest, with the magnitude of these specific neurophysiological changes being mirrored by individual gains in untrained WM performance.*”
- ▶ **Noteworthy:** There was **considerable individual variation** of magnitude of change in WM before and after Cogmed. Individuals varied in the amount of change in WM, but **increased WM capacity correlated with the degree of increased neural connectivity.**



Figure 3: Functional Interaction between group/time (A - Green) & Changes in Connectivity for Groups (B) & WM/Connectivity for Individuals (C).

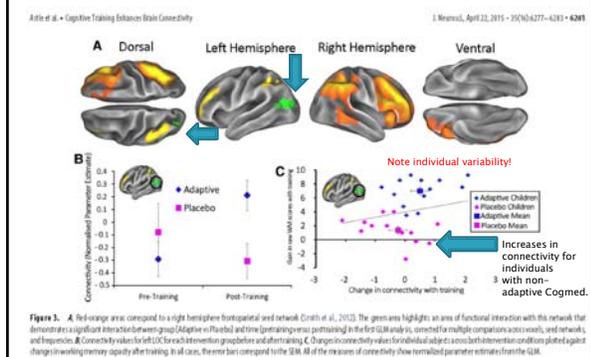
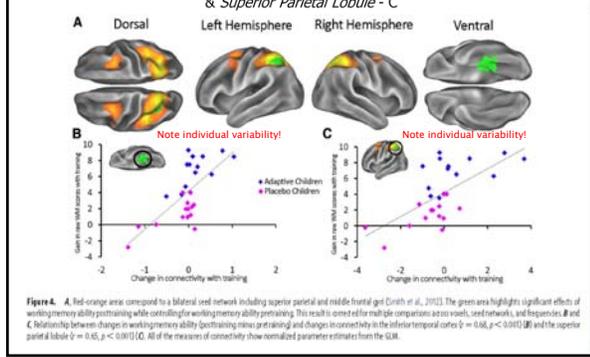
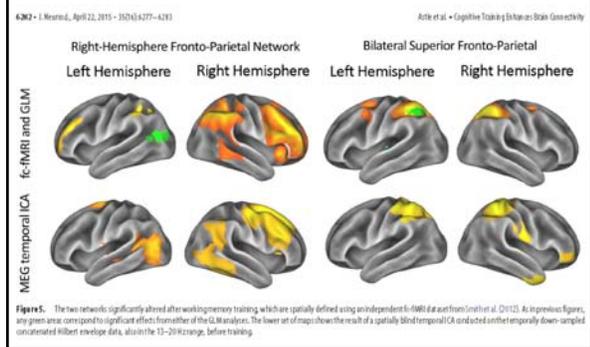


Figure 4: Significant effects of WM ability post-training while controlling for pre-training ability (Green) Changes in WM ability - A & Changes in Connectivity for Groups at the Inferior Temporal Cortex - B & Superior Parietal Lobule - C



Green Indicates Networks Significantly Altered Post Cogmed from fMRI data set from Smith et al., (2012)



Astle, et al., (2015) Deepens the Evidence that Cogmed Results in a Change in WM Capacity

- ▶ Due to the measureable difference in brain activity while at rest post **training the gains from Cogmed cannot be attributed to motivation or strategy since one is not engaging in any activity while at rest.**
 - Response to critics alleging improved strategy use and varying motivation explain improvement performance while claiming that there is no "actual increase in WM capacity" from training.
- ▶ This biophysical indicator of increased neuronal connectivity consistent with and correlated to the behavioral change of increased WM capacity deepens the evidence indicatino a brain-behavior basis of change.



Individual Variability Implications of Astle, et al., 2015

1. **Variability of individual results often appears to be overlooked and underplayed by researchers and clinicians who instead emphasize group level differences.** Yet, individual differences is also a reasonable explanation for a lack of findings in some studies. This issue along with ignoring severity of disorders and impact of comorbidity.
2. **Implications of only considering group level differences:**
 1. Group level differences are clinically meaningful and important.
 1. This informs expectations for interventions with groups.
 2. This also becomes the rationale for administering Cogmed at a class or group level.
 2. **Obscures important individual differences.**
 1. Superlative gains that could be argued to change the whole developmental trajectory of some who do Cogmed training may be lost in group data.
 2. Superlative gains are not likely to be a reasonable expectation of all those who train.
 3. Some individuals may make significant, but not superlative gains.
 4. Some samples may require adjustments in 'dosing' to deliver greater gains. This can be the case in those with more severe disorders, greater comorbidity, more severe WM deficits, intellectual disability, etc.



Individual Variability Implications of Astle, et al., (2015)

1. **Individual Differences Implications:**

Subject variables may help us to better understand individual variation in gains.

 1. Closer scrutiny of individual differences among subjects may help us to better account for variation in gains independent of coaching (e.g. mindsets (Dweck), etc.)
 2. This suggests the pragmatic likelihood that training may work better for some individuals than others. Understanding this has implications for training which may include 'dosing' issues or the amount of training overall.
2. **Coaching Implications:**

Better understanding how to facilitate these "optimal gains" suggests a closer scrutiny of components of coaching effectiveness and individual differences.

 1. Coaching components may be essential for optimizing gains.
 2. It also suggests that certain types of coaches or coaching with certain components is more effective with certain trainees.



Coaching Implications of Astle, et al.,(2015)

One would presume that maximizing gains would be paramount.

One might hypothesize that coaching might facilitate greater gains and thereby highlight the role of coaching.

One may also hypothesize that individual differences may predict greater gains.

Both these avenues of inquiry for future research could give clearer clinical and educational parameters for maximizing gains.



Brain Implications for Astle, et al., (2015)

▶ "Previous studies of the neuro-physiological mechanisms of attentional control and working memory have highlighted the importance of long-range functional connections."

• *Such connections were enhanced post Cogmed in this study.*

▶ "Moreover, these enhancements occur at a frequency previously associated with attentional control mechanisms (Hanslmayr et al., 2011)."

• *"Cognitive training was associated with altered connectivity within the 13-20 Hz frequency."*

▶ "These same top-down modulatory signals are also present at different stages of working memory encoding, storage and retrieval (for review, see Gazzaley and Nobre, 2012)."

• *The salience of working memory to encoding has been argued on a conceptual and construct level this supports this relationship on a biomarker level.*

Brain Implications for Astle, et al., (2015)

▶ "This study represents the first systematic demonstration that cognitive training augments intrinsic neurophysiological brain connectivity in childhood."

▶ "Furthermore, because we use MEG, which is a direct measure of neural activity, our effects cannot be attributed to differences in blood flow or metabolism (Schmithorst et al., 2015)."



Astle, et al., 2015 Explanation of WM Capacity Gains:

"We suggest that working memory training may result in capacity gains because it intensively taxes these control mechanisms, resulting in their enhancement. This *enhancement is apparent even at rest* in the endogenous coordination of activity between areas in fronto-parietal cortex and areas in inferior temporal cortex (close to area IT) and LOC. Moreover, these enhancements occur at a frequency previously associated with attentional control mechanisms (Hanslmayr et al., 2011).



Why does resting state functional connectivity matter?
(Barnes, Woolrich, Baker, Colclough & Astle, 2015)

- ▶ "Functional connectivity is the statistical association of neuronal activity time courses across distinct brain regions, supporting specific cognitive processes."
- ▶ "Some of these functional connections are identifiable even when relevant cognitive tasks are not being performed (i.e. at rest)."
- ▶ "We used magnetoencephalographic recordings projected into source space to demonstrate that resting state networks in childhood have electrophysiological underpinnings that are evident in the spontaneous fluctuations of oscillatory brain activity."
- ▶ "Using the temporal structure of these oscillatory patterns we were **able to identify a number of functional resting state networks analogous to those reported in the adult literature.**"

Why does resting state functional connectivity matter?
(Barnes, Woolrich, Baker, Colclough & Astle, 2015)

- ▶ "...**the strength of connectivity** between a fronto-parietal network and lower-level processing areas in inferior temporal cortex **was associated with spatial working memory capacity**, as measured outside the scanner with educationally relevant standardized assessments. "
- ▶ " *This study represents the first exploration of the electrophysiological mechanisms underpinning resting state functional connectivity in source space in childhood, and the extent to which the strength of particular connections is associated with cognitive ability.*"
- ▶ *In short, behavioral changes were registered in brain changes.*

Why does resting state functional connectivity matter? (Barnes, Woolrich, Baker, Colclough & Astle, 2015)

IMPLICATIONS:

- Effects of Cogmed in Astle, et al., (2015) *cannot be explained away as an expectancy effect.*
- *The change found is not simply the subjective view of subjects, coaches, parents or teachers.*
- Since changes were found at rest suggests it cannot be explained by greater strategy use, but an actual increase in capacity is a more reasonable explanation.
- Greater WM capacity was associated with greater connectivity in Barnes, et al., 2015.
- In the Cogmed-specific study, Astle, et al., 2015, greater gains in WM capacity and greater connectivity AFTER COGMED was found.
- Hence the conclusion is that this is very strong data to suggest that:
 - Cogmed leads to gains in WM capacity reflected in changes in neuronal functioning.

Summary

- ▶ From the outset Cogmed researchers explored the physiological basis of brain training.
- ▶ Olesen explored areas of the human brain activated by Cogmed WM training with MRI.
- ▶ McNab explores the biochemical changes using PET scans
- ▶ Westerberg et al examined changes as a result of dopamine and gene phenotypes.
- ▶ Soderqvist et al reviewed the dopamine transporter system
- ▶ More recently researchers have used EEG recordings to show changes in electrical activity of certain types of brain waves. (2015)

Summary & Implications

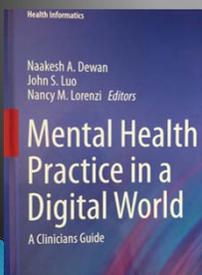
- ▶ Astle, et al., 2015 findings showed that improved WM capacity correlated with increased brain connectivity at rest. There was notable individual differences in both gains in WM and increases in connectivity. There are many implications for these MEG findings. One is that increased capacity is anchored in brain.

Summary

- ▶ Individual differences found in Astle, et al., 2015 have implications for the interpretation of the results of all Cogmed studies.
 - This individual variability is consistent with the arguments of Shinaver & Entwistle that severity of disorder and co-morbidity are quite likely moderators of gains in Cogmed.
 - These findings expand this argument into the typically developing population.
 - This means that by ignoring individual variation among groups in Cogmed studies we may obtain a reasonable explanation for the lack of findings or limited findings in some cases.
 - Similarly severity of disorder and/or co-morbidity are also reasonable explanations for a lack of findings or limited findings.
 - Individual variability also suggests the plausibility of 'dosing' of the amount of training could be key to reaching those with more severe disorders and/or co-morbidity.

Book Chapter published by Charles & Peter in
 "Mental Health Practice in a Digital World"
 Our chapter: "Computerized Cognitive Training Based upon Neuroplasticity."

Please [Click Here](http://www.springer.com/us/book/9783319141084#) or go to this URL:
<http://www.springer.com/us/book/9783319141084#>



This chapter puts into the larger perspective computerized cognitive training in the areas in which it has been most applied clinically: Schizophrenia, Traumatic Brain Injury & ADHD.

It is in this chapter where the "severity of disorder" argument is made.

Our Other Publications since 2013

Shinaver, C. S., III, Entwistle, P. C., Soderqvist, S. (2014). **Cogmed Working Memory Training: Reviewing the Reviews.** Applied Neuropsychology: Child.

Entwistle, P.C & Shinaver, C. S. III (2013). **Working Memory Training & Cogmed.** In S. Goldstein, & J. Naglieri (Eds.), *Handbook of Executive Functioning.* New York, NY: Springer.

