Cogmed Working Memory Training

Claims & Evidence – Extended Version
V.4

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Introduction

Working memory (WM) involves the ability to focus on a task, keep information in mind and to do mental processing of that information. It is a fundamental brain function that underlies most of our conscious mental work. WM is required in order to understand the content while reading and it is the brain's work space when solving a math problem. It is used when following instructions, reading a map or simply carrying on a conversation. It is limited in its capacity and sensitive to distractions. Impairments in WM are often seen in individuals with ADHD, acquired brain injury and many other common conditions resulting in difficulties with concentration and learning. This in turn may lead to behaviour issues, feelings of low self-confidence and social problems. Until earlier this century, it was presumed that WM capacity was a trait that was rather static, so that once adult maturation of the brain was reached, the WM capacity would be fixed. Based on neuroscientific findings indicating plasticity of the areas of the brain that encompass WM capacity, an innovation from the Karolinska Institute in Sweden was born, demonstrating that WM could in fact be trained to enable more and better information processing (1-4). These discoveries were the foundations on which Cogmed Working Memory Training (CWMT) was created.

CWMT has since continued to develop as an evidence-based intervention and great care is taken to ensure that the claims that are made by Cogmed regarding the effects are supported by published research. As of March 2016, there are 80 original research studies examining the effects of CWMT published in peer-reviewed journals. The effects demonstrated in those are the basis for the claims that Cogmed currently makes. This document describes the policy underlying the formation of a Cogmed claim, as well as an elaboration of the evidence supporting each claim.

The importance of WM in everyday life, in learning, and information processing is self-evident, and makes WM training both relevant and compelling to pursue. While WM capacity itself is relatively easy to quantify using standardized laboratory measures, assessing it and related functions in everyday life is much more challenging. The lack of instruments that can quantify a change in the number of WM related failures occurring during a classroom lecture, a phone conversation, a meeting, or a shopping run to name a few examples, is a reality and a boundary within which the evidence base lies. While the technology to track brain activity and function in everyday situations, across large periods of time may be within a theoretically possible grasping point, it is far from the reality of where the academic research field currently operates. Despite this limitation, evidence of benefits related to CWMT in everyday situations is emerging.

Methodological considerations

Control groups

For a study to be able to adequately answer the question of interest it is important to have a control group to which any changes in performance or behaviour can be contrasted. In the case of CWMT this typically includes controlling for test-retest improvements, that is improvements in test performance that occur when the test is repeated. This is controlled for in studies using active control designs and in studies using a waitlist or passive control, where both the active training group and the comparison group perform the test before and after the intervention period. The design of using an active control group also controls for the time spent with the intervention as well as time spent interacting with researchers or other contact persons. The type of design that is optimal for a study depends on the question(s) being asked. For example, if one wants to compare an intervention with the treatment a person would typically receive, then a treatment as usual, or waitlist control group is valuable. This will answer the question of whether an intervention is a valuable addition to the a person's well being. However, if one wants to answer more specific questions concerning specific components of an intervention, then one needs to have an active control condition where all components except for the one of interest are held the same, or as similar as possible. In initial studies of CWMT, researchers were particularly interested in investigating the adaptive component of training and therefore used a program that was identical to normal CWMT except for the adaptive level algorithm. Since the initial studies were published the effect of adaptive WM training has been well demonstrated and the use of a non-adaptive control is not necessarily optimal for studies investigating other aspects of CWMT.

Inferential statistics

In statistical analyses, one hopes to make inferences about a certain population. Since it is most often impossible to test the whole population of interest, one must draw a smaller study sample that is assumed to reflect this population. However this is not always the case and it is impossible to know whether a sample is or is not reflective of the population as a whole. When a hypothesis is posed in an experiment there are two types of risks for drawing false conclusions that stem from a discrepancy between the sample population included in the study and the larger population of interest. A Type I error (or false positive) means finding an effect that is not actually there in the population as a whole. The probability of making this type of error is usually designated by α. A Type II error (or false negative) means failing to find an effect that is actually there in the population as a whole. The probability of making this type of errors is usually designated by β. The general statistical convention is to allow a maximum α of 5% (risk for a Type I error) and a maximum β of 20% (risk of a Type II error).

Type I error

In the case of intervention studies, the risks associated with drawing false positive conclusions are that interventions that are not actually effective will be deemed as effective, possibly causing people (more research/funding/individuals) to "waste" their time and money with little or no benefit as a result. This is of course of ethical concern and is one of the reasons to why the α level is set rather low (5%). In studies where many independent tests (on independent data sets) are run, the risk of a Type I error increases (for the study as a whole). One can decrease this risk by setting an α level cut-off that is even lower using a method for correcting for multiple comparisons (e.g. Bonferroni correction). However, this is sometimes done also when the tests are not independent, causing the α to be unnecessarily strict and consequently increasing the risk of a Type II error.

Type II error

The consequence of drawing false negative conclusions are equally problematic. In the case of intervention studies, this would imply that a research study concludes that there is no real effect following an intervention, when in fact the intervention is effective in the population as a whole. This could mean that individuals/clinicians/researchers would be discouraged from pursuing the intervention, leading to missed remediation or further exploration of the findings. This is of ethical concern as it may discourage development and further pursuit in effective treatments or interventions, causing the progress within a research field to stagnate. Consequently, it may withhold useful remediation from individuals who would benefit from it.

The statistical power of a study ($1-\beta$) which is the probability of finding a true effect, is affected by the study sample size, the effect size and set α level. A study is considered “underpowered” when the sample size is too small considering the expected effect sizes, leaving the study with a low probability of identifying real effects that would be observed in the whole population. Therefore, it is of ethical importance not to overstate the impact of non-significant findings *if the study is underpowered to detect relevant effect sizes*. Thus, one should always consider effect sizes in addition to the statistical significance (α) using for example methods of meta-analyses.

While such methodologies have advantages in terms of their rigour, they do not always meet demands of summarizing results more swiftly. Due to the quickly evolving literature on CWMT, Cogmed employs a policy to evaluate evidence from studies including a set of criteria for when such evidence is to be considered sufficiently strong for Cogmed to support a claim. These are stated below.

Evaluation of research and formation of claims

General quality of research

For a study to be considered to be of sufficient quality to contribute to formation or revision of a claim, the criteria listed below must be met. These closely match the criteria listed for evaluation of “effectiveness of research based psychotherapies for youth” by Silverman & Hinshaw (2008).

- Reliable and valid outcome measures
- Design that supports the hypothesis
- Statistical methods that support the question being investigated
- Study on recommended population according to Cogmed training manual (excluding studies where majority of sample has severe oppositional disorder, high comorbidity, intellectual disability (IQ <70), severe depression or anxiety).
- Implementation with high fidelity to Cogmed recommendations regarding coaching method, study population, and high quality of training.

Formation of a claim

Randomized controlled trials (RCT) and controlled studies that investigate the effects of CWMT and meet the standards above for quality will be considered when forming a claim. Criteria for forming a claim are as follow (at least one out of the three must be fulfilled):

- An effect is observed in at least two RCTs.
- An effect is observed in at least three controlled studies.
- An effect is observed in one RCT and in two controlled studies.

Disputable results of effects

Claim criteria: Assuming that the probability of making a Type I vs Type II error is set to the conventional cut-off levels (maximum α of 5% and maximum β of 20%), it is Cogmed policy to revise a claim when at least three studies with sufficient power to detect a medium effect size and overall quality fail to replicate a previously established effect.

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Cogmed Claims

Based on the above criteria and assuming good fidelity to the Cogmed method, Cogmed supports the following claims:

1) CWMT leads to sustained improvements in working memory, from childhood to adulthood (M2, M5), as seen in
    a) preschoolers (6, 16, 41, 42, 61)
    b) children and adolescents (1, 3, 7, 13, 18, 25-27, 33, 34, 36, 45, 50, 52, 53, 62, 64, 66, 72)
    c) adults and old adults (5, 15, 22, 28, 37, 38, 46, 47, 68, 70, 71)
2) CWMT leads to sustained improvements in attention (M3, M5) seen in both
    a) subjective measures of attention (3, 11, 14, 18, 38, 31, 47, 66, 72)
    b) and objective measures of attention (5, 6, 15, 22, 25, 28, 66, 72)
3) Improvements in working memory following CWMT are associated with changes in functional brain activity
    a) seen as changes in the neurochemistry (9), functional activity related to working memory (2, 4, 22, 59), and functional connectivity at rest (52)
4) Learning outcomes in reading (13, 35, 45, 69) and math (34, 43, 45, 69) improves for many students following CWMT
5) In clinical trials, CWMT has been shown to improve attentional problems in many with ADHD
    a) as evident in rating scales (3, 11, 47, 72)
    b) or measured with objective measures (25, 72)
6) Research studies of CWMT report improved cognitive functioning in daily life (28, 47, 71, M3, M5)
7) Adults with acquired brain injury report reductions of symptoms after CWMT in clinical trials (5, 15, 37, 38)
8) Improvements on measures of cognitive control have been demonstrated in studies after CWMT (1, 3, 41, 72, M5)

"M" signifies that the claim is also supported by the results from a meta-analysis.

Elaboration of the evidence underlying each claim

This section discusses each of the claims and highlights specific findings that are especially impactful given the design or methods used in the particular studies.

Claim 1

CWMT leads to sustained improvements in working memory, from childhood to adulthood (M2, M5), as seen in

a) preschoolers (6, 16, 41, 42, 61)
b) children and adolescents (1, 3, 7, 13, 18, 25-27, 33, 34, 36, 45, 50, 52, 53, 62, 64, 66, 72)
c) adults and old adults (5, 15, 22, 28, 37, 38, 46, 47, 49, 68, 70 71)

The claim that CWMT improves WM is at the very core of the purpose of this training method and is supported by 35 controlled studies and is well substantiated through independent meta-analyses using analyses specific to Cogmed studies (M1, M2, M3, M4, M5). This was first demonstrated in the original studies by Klingberg and colleagues (2002 and 2005) which ultimately took this research innovation from the Karolinska Institute (Stockholm, Sweden) to be available commercially. This has since been replicated by independent research groups worldwide in studies of high methodological rigour (blinded, randomized controlled trials) (16, 25-27, 33, 41, 50, 62, 64, 66, 68, 70, 71, 72). The fact that WM is proven to be malleable with practice is a groundbreaking finding, which has caused some resistance and controversy in the academic world of psychological theory in which WM capacity had traditionally been viewed as a fixed trait (Shipstead et al, 2012 and subsequent commentaries). In the 2012 Cogmed Research Meta-analysis, which included all Cogmed studies published at that time, research participants in the standard adaptive Cogmed training group improved an average 26% in visuo-spatial WM and 23% in verbal WM more than the control groups from baseline to post-test on non-trained WM tests (available from the Cogmed website, cogmed.com/research). One published meta-analyses showed that improvements in WM following CWMT were of large effect sizes (d = 1.18 in verbal and d = 0.86 in visuo-spatial) (M2). Furthermore, in comparison with other WM training programs, the effects seen after Cogmed were larger than all other interventions. This finding has since been reproduced in a larger meta-analysis with more than 100 studies (M5). Thus, the research evidence for Cogmed has consistently demonstrated significantly improved WM.

WM assessments

The outcomes that have been used to assess WM have included tasks that are similar to the trained ones for instance Digit span backwards for verbal WM and Block tapping task for visuo-spatial WM, only presented in a different manner (e.g. physical blocks) and using a verbal response to answer (for digit span). This is done in order to minimize the use of task specific strategies that one may have developed during the training. The effects have also been shown on tasks that are more dissimilar to the trained ones, sometimes including a more complex processing operation than simply reproducing or reversing a sequence (7, 8, 16, 31, 43, 46, 64). This ensures that the WM increases seen after training are not entirely task-specific but transfer to tasks that do not allow use of the same strategies as those potentially used during training.

Populations studied

The populations studied with CWMT that have demonstrated improved WM capacity include samples of ADHD (1, 3, 13, 25, 27, 34, 36, 42, 43, 47, 49), brain injury, (5, 15, 26, 37, 38), low WM/ at risk for academic underperformance (7, 18, 33, 41, 50), typically developing/developed (6, 16, 22, 28), children born prematurely (14, 30), children with intellectual disability (31, 63), with epilepsia (64), with anxiety (78), adults with Mild Cognitive Impairment (58, 71) and methadone maintenance users (68). Whether the magnitude of WM improvements related to training depends on whether WM was low or in the normal range prior to training is yet unclear (see 20, 45, 24 for examples of this type analysis). The impact of CWMT on daily life, is however likely to be more pronounced if WM deficits are underlying behavioural problems, academic difficulties or other cognitive deficits (see claim 2, 5, 6 and 7 for further discussion).

Sustained effects

The effects on WM after training have been shown to be sustained where follow up assessments have been conducted at 2 to 12 months post intervention (3, 7, 14, 18, 33, 36, 37, 41, 47, 61, 71). This has also been concluded when the sustainability of the effects in studies evaluating CWMT have been summarized in meta-analyses (M2, M5).

Claim 2

CWMT leads to sustained improvements in attention (M3, M5) seen in both

a) subjective measures of attention (3, 11, 14, 18, 38, 47, 66, 72)
b) and objective measures of attention (5, 6, 15, 22, 25, 28, 66, 72)

As previously mentioned, studying attention and WM in the laboratory is generally reliable, but quantifying it in everyday situations is more difficult. The effects of CWMT on attention have been demonstrated on two levels; subjective and objective. The subjective measures consist of questionnaires regarding attention difficulties either directly for the trainee, or for someone close to the trainee (parent or teacher), to rate. This is done prior and post training and is then compared with the equivalent data from a control group (who received either a comparison intervention or no intervention) (3, 11, 14, 18, 26, 38, 47, 66, 72). The objective measures of attention are either laboratory measures of sustained attention (5, 6, 15, 22, 28, 66, 72) or observational data from blinded raters assessing student’s abilities to stay on task during an academic performance task (25).

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Subjective measures of attention
A large meta-analysis of more than 100 studies (M5), out of which specific analyses were performed to tease out the effects of Cogmed (30 studies), concluded that there were significant improvements on measures of everyday functioning and concluded that WM training is relevant and efficient.

> "Most important, the enhanced function of the system is reflected in the better performance of everyday life tasks and reduces disease-related symptoms in patients suffering from WM deficits" (Weicker et al., 2015, p. 14).

The positive effect of training has been observed on improvements on parental ratings of inattention including the DSM-IV Parent Rating Scale, DuPaul ADHD-RS-IV, Brief Inventory of Executive Function (BRIEF), Disruptive Behavior Rating Scale (DBRS), and Conner's Parent Rating Scale, as well as by teacher ratings on Strengths and Difficulties Questionnaire (SDQ), and the DuPaul ADHD-RS-IV (School version). Adult users have also reported significant decreases in their own symptoms and improvements in daily life using the DSM-IV Adult Rating Scale, Cognitive Failures Questionnaire (CFQ), and the Canadian Occupational Performance Measure (COPM) (see Claim 6 and 7 for further information).

Objective measures of attention
The laboratory tests of attention that have been used in studies where effects of CWMT has been demonstrated include the Paced Auditory Serial Addition Task (PASAT) (5, 15, 22, 28) in adults and a type of Continuous Performance Task (CPT) (6, 66, 72) in children. The PASAT involves presenting a series of single digit numbers where the two most recent numbers must be summed. It is considered to be a measure of sustained attention. The Auditory Attention test (NEPSY-II) assessing the same ability adapted for children includes presenting auditory cues for the child to respond to certain ones while ignoring others. One study examined attention while the students performed an academic task (RAST) and found that individuals who had trained CWMT, on average had fewer instances of lapses in attention, primarily looking away from the task and playing with an object

during the task, compared to an active control group (25). This effect was found when the student's behaviour during this task was rated by assessors that were blind to each student's training condition (Cogmed or control). These effects clearly illustrate how inattention may directly impair academic performance.

Sustained effects

In a meta-analysis (M3) reviewing results on ratings of attention from studies investigating the effects of CWMT (Spencer-Smith & Klingberg, 2015), it was concluded that there is a small to moderate effect (d = 0.37) on ratings of inattention and that this effect is largely sustained 2 to 8 months later (d = 0.33).

Claim 3

Improvements in working memory following CWMT are associated with changes in functional brain activity

a) seen as changes in the neurochemistry (9), functional activity related to working memory (2, 4, 22, 59), and functional connectivity at rest (52)

Effects of CWMT on a more fundamental neuronal level have been studied using functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and Magnetoencephalography (MEG). fMRI serves as a proxy for measuring brain activity. It provides a blood- oxygen-dependent (BOLD) signal, which reflects oxygen levels in the blood. Since an increase in oxygen level is related to increased brain activity, it is assumed that the BOLD signal can be used as a non-invasive measure of brain activity. Studies using fMRI to measure effects of CWMT typically include measuring brain activity of participants in both the active training group and in the control group before and after the training period. This way the researchers can get an objective estimate of how the brain activity has changed after training and to which extent this change is due to completing CWMT. So far four different studies have used this method to investigate changes in brain activity relating to CWMT (2, 4, 22, 59). These studies, including young and older adults have all shown alterations in activity in WM related brain areas following training. These findings show that CWMT influences how the brain processes information in a WM demanding task, and the degree of influence to be directly related to the degree of improvement during CWMT. Thus, the evidence suggests that the improvements seen during CWMT are directly related to changes observed in brain activity.

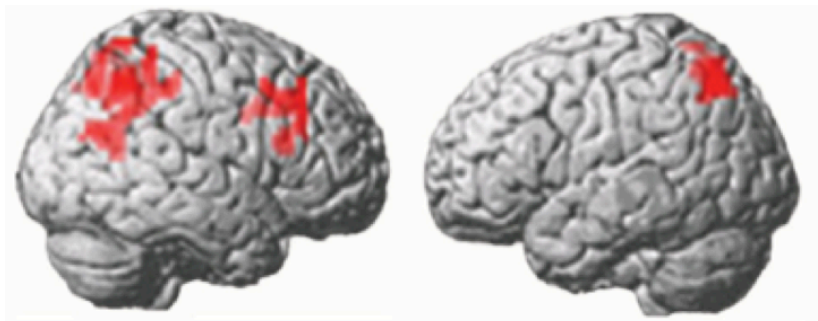

Figure 1. Brain areas demonstrating changed activity following CWMT from the study by Olesen et al. (2).

In 2009 a study by McNab and colleagues (9) was published in the prestigious scientific journal, *Science*. This study demonstrated that CWMT influences the brain's neurochemistry, in particular its dopamine receptors. Using PET to measure the density of dopamine receptors in the brain before and after training, the researchers found that CWMT altered the density of dopamine D1 receptors, again observing a relation between degree of improvement during training and degree of alteration of receptor density. Thus this study demonstrates that CWMT influences fundamental neurochemical properties of the brain. Influence of the dopaminergic system of the brain is of particular relevance for WM and WM training since dopamine is known to be crucial for both WM and attention and is the primary target of psychostimulants used to alleviate symptoms of ADHD.

One study by Stevens et al. from Yale University (59) using fMRI to investigate training related changes in the brain in a sample of children with ADHD showed that the changes observed in the brain after CWMT were linearly related to the reductions seen on ADHD symptoms. This indicates that the training induced functional changes in the brain and that the degree of change was related to the improvements seen in behaviour.

Another method for measuring brain activity is MEG, a sensitive measure of changes in the magnetic field occurring as a result of the electrical signals that underlie brain activity. Astle and colleagues (52) used this method to measure functional connectivity, that is the way in which different areas of the brain synchronise their activity over time. In this randomized and controlled study (using Cogmed non-adaptive training as a control) they demonstrate significant changes in resting-state connectivity following CWMT. In addition the authors identified a substantial variance in improvements of WM following training and demonstrate that the neurophysiological changes observed were directly related to level of improvements in WM following training. The type of long-range connectivity they investigated has previously been demonstrated to be important for WM and attentional control, and is believed to be crucial for dynamic regulation of ongoing processes. Because measures are taken while children are at rest (not performing a task), the differences observed cannot be explained by differences in strategies, motivation or other task-specific skills.

Claim 4

Learning outcomes in reading (13, 35, 45, 69) and math (34, 43, 45, 69) improves for many students following CWMT

Immediate and delayed effects

In recent years, academic performance has been measured in an increasing number of studies following CWMT. Some studies have shown significant academic improvements directly following CWMT (13, 35, 43) while others have not seen any effects (7, 33, 50, 80) or not shown statistical significance of the effects (32, 62, 75), compared to a control group.

Reading
Out of the studies investigating the effects of CWMT on reading ability, there are four controlled studies that have reported significant effects after training. One randomized, controlled trial (35) that investigated the effects of CWMT training on reading in children aged 10 to 12 with ADHD reported a medium effect (d = 0.46) on a reading comprehension test (LOGOS Reading Fluency) directly after training which was retained and slightly increased (d = 0.62) at the 8 month follow up. There were also significant effects on a test measuring decoding quality directly after training (d = 0.57) which was also maintained 8 months later (d = 0.64).

A similar study by Dahlin (13) found effects in a sample of 9 to 12 year old children with attention difficulties and special needs, on a measure of reading comprehension (from the Progress in International Literacy Study, IEA) compared to controls. The magnitude of the effects was large directly after training completion (d = 0.88) and was maintained (d = 0.91) at the 7 month follow up assessment.

One study by Holmes & Gathercole (45) investigated the effects of CWMT as a teacher lead intervention implemented as part of the classroom activities (45). After demonstrating the feasibility of implementing CWMT in the classroom in a first sample, they then let two different samples of children with low academic achievement, in grades five and six train CWMT and followed their academic school progress at the end of the school year. They used the National Standard Assessment Test (SAT) in English (reading, writing, speaking and listening skills) as the outcome and reported a medium to large effect (*d* = 0.67) in the sixth graders (but not the fifth graders) along with significant effects in math performance (see below). The researchers reported that "Children improved in math and English compared with matched control group and out of the training group 84% achieved the national expected levels of attainment in English compared to 72% in the control group."

One randomized, controlled trial by Foy & Mann (41) has investigated pre-reading markers in a group of children between the ages of four and six at risk for academic underachievement. They reported a medium effect (*d* = 0.51) on a test of phoneme awareness (First Sound Fluency Test, DIBELS

Next) three months after training completion compared with controls (statistically significant at trend level).

Similarly, a study investigating effects of CWMT on reading acquisition in a sample of typical seven-year-olds demonstrated large effects on word decoding which was retained and increased two months later (75).

Finally, a recent study tracked the academic development across two years for two typically achieving classrooms in the same school where one class had received CWMT and the other had not (69). The Cogmed class showed a significantly steeper development on a standard reading test than did the control classroom with an effect size of 0.66.

One important factor to remember when investigating WM and learning outcomes is the fact that WM is only one part of the puzzle. CWMT should not be considered to be a replacement of formal instruction or practice of reading because many other more important factors such as phonological awareness, decoding skills etc. determine reading ability. WM may be more or less involved depending on the origin of the difficulties. A likely explanation to the findings indicating a growth in reading performance over time is that in those cases where an impaired WM has been limiting performance in reading, effects are apparent in conjunction with the increases in WM capacity. However, for those where WM has not acted as a bottleneck for applying current knowledge to performance, effects may not be evident immediately after training, but may emerge in the months following training as an increase in WM capacity enables more learning opportunities and more efficient practice. This is an explanation that would encompass effects in school-aged children where formal instruction and practice are taking place. It is perhaps less likely to be observed in adults who are not currently learning to read or developing their reading proficiency which may explain the non-effects in the study of adults by Gropper et al. (47) and Mawjee et al. (65).

Math performance

There are a few controlled studies that have reported significant effects on math performance after CWMT. In the study by Dahlin (34) from 2013, performance on a test of math concepts (Basic Number Screening Test including grouping, number concepts, serial number patterns, arithmetics, value, division) was compared between controls and Cogmed completers in 9 to 12 year old children with attention deficits and special needs. The effects seen directly after training were in the medium to large magnitude (*d* = 0.69) and these effects were maintained at the 7 month follow up (*d* = 0.65). The study also reported a non-significant effect size of *d* = 0.55 on speeded addition directly following training which was partially maintained (*d* = 0.33) at follow up.

The study by Holmes & Gathercole investigated the effects of CWMT as a teacher lead intervention implemented as part of the classroom activities (45). After the two different samples of children with low academic achievement in grades five and six completed their Cogmed training the researchers assessed them and controls at the end of the school year. They used the National Standard Assessment Test (SAT) in math (assessing how to use and apply maths, algebra, shape space, measures and handling data) as the outcome measure. When comparing the academic attainments across the year for the CWMT groups with an age matched sample, the effect sizes for math performance were large and medium (*d* = 1.15 and 0.6, for grade five and six respectively).

One large scale study by Bergman Nutley & Klingberg investigated the training effects on speeded arithmetic performed as part of the Cogmed Progress Indicator (CPI) in Cogmed users during and directly after training and compared them with age-matched controls who only performed the CPI tasks five times over the course of 5-7 weeks (43). The trained sample all had deficits in WM and showed large improvements on the WM tasks with training. The improvements seen on the math task was small to medium (*d* = 0.44) and this improvement was linearly related to the improvements seen on the Following Instructions task. This study did not include a follow up assessment.

In the previously mentioned study tracking Cogmed users for two years post training there was also a steeper development demonstrated for math, compared to the control classroom (69) with an effect size of 0.58. The degree of this development was in linear relation to the degree of WM improvement demonstrated on the Cogmed Progress Indicator (CPI) two years earlier.

A likely explanation to these findings indicating a growth in effect over time is that for aspects of maths performance that rely heavily on WM, effects may be apparent immediately when more information can be retained and processed in WM. For learning new skills, these effects will naturally rely both on the math instruction taking place and the ability to learn that new information, where WM plays an important part.

Out of the studies that did not find significant effects on reading or math performance after training, there is only one powered appropriately to be reliable in terms of the results (80). This was a large scale, randomized controlled trial that implemented Cogmed in a multi-site school study on six-year-olds in Australia. The purpose was to investigate whether Cogmed would provide a cost efficient way of improving academic growth in children with WM deficits. They screened for WM deficits and trained 226 six-year-olds with the standard Cogmed RM protocol (50 min, 5 days/week for 5 weeks). The results showed that WM was improved and that effects were sustained for up to one year, but there were no benefits evident on standardized ability tests of reading or maths, one and two years post intervention. One factor that may be of importance when studying academic growth is the type of instruments (choice of standardized ability test, and materials and tests selected by the schools) used to assess growth. The properties of standardized ability tests for academic achievement determine their utility and while some tests may be excellent in identifying those with severe problems (screening), they may not be appropriately sensitive to detect subtle change in the normal range. As academic performance depends both on the ability to learn (which would be the working memory related part) and the degree of academic skill instruction and practice taking place it may be that in order to assess a change in the ability to learning, one has to assess performance over time on the actual materials or areas being studied in the time since the intervention.

Another important point that differs between studies that may influence the results is the age at which training is performed. All of the studies reporting effects on academic performance have been on children with a mean age of

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nine or above and the two studies investigating effects on early literacy on younger children (aged 4-7) have used phoneme awareness (Foy & Mann, 2014) and decoding of words (resulting in medium to large effect sizes) (Fälth, 2015) as pre-reading markers instead of actual reading ability. Thus the effects of CWMT on academic performance might be specific to both age group and the type of academic performance being measured. Possibly, due to the otherwise dramatic and noisy development occurring during the earliest years of schooling, CWMT might not have a significant impact in children who are not explicitly hindered in their learning by a WM deficit.

Since WM's role in learning is evident, it is of utmost importance to respect the properties of this outcome. Learning is not an absolute state, but a process that occurs over time and if one intends to affect learning one must find a proxy that can be measured over time (e.g. reading comprehension) to demonstrate the change in performance relative to a comparison condition which did not receive the hypothetical impact on learning. Many more factors in addition to WM determine academic growth and to investigate the specific contribution of WM training on learning, one needs to carefully control all other influences on learning, for instance; the degree to which they are taking part in learning after the training, the content of that learning, the quality of that learning experience, the characteristics of the sample (adult vs. child, ADHD vs. typical) etc. A difficult and expensive challenge for the research field to tackle but one that needs to be addressed with large scale, randomized controlled longitudinal trials of each age and population type before any generalizable conclusions can be drawn in regards to WM training's impact on learning. The current evidence seems to suggest that many, but not all, benefit on measures of academic performance after CWMT.

Claim 5

In clinical trials, CWMT has been shown to improve attentional problems in many with ADHD

a) as evident in rating scales (3, 11, 47, 72)

b) or measured with objective measures (25, 72)

WM deficits are commonly observed in patients with ADHD and WM has been suggested to be a core function underlying ADHD symptoms. This has motivated a number of studies to investigate the effects CWMT has on ADHD symptoms overall and inattention in particular.

Rating scales

The first large study using Cogmed to be published was by Klingberg and colleagues in 2005 (3). This study included children aged 7-12 who were diagnosed with ADHD. Children with co-morbid diagnoses and/or who were taking psycho-stimulant medication were excluded. Results showed significant improvements in symptoms of inattention as reported by parents of the participants. The improvements following training were found to be significantly greater for the adaptive training group when compared with a non-adaptive control group, and these effects remained significantly greater when measured again 3 months after training had been completed. Positive effects on symptoms of inattention in patients with ADHD has later been replicated in both children and adolescents as rated by parents (11) and in self-ratings in adults (47). One study on 5-7 year-olds with ADHD reported a significant relation between the improvements on the WM tasks (index improvements) and the reduction of symptoms as rated on two scales by teachers (BRIEF and ADHD-RS), however effects were not evident on a group level in comparison with an active control group (training at level two) (42). A later study investigated effects of CWMT in a sample of children with ADHD aged 7-12 years, using a double-blind, randomized controlled design with a control group training with the CWMT non-adaptive version (72). Directly following completion of training and 6-months later participants' parents and teachers rated behavioral problems of the participants. Results show sustained improvements on the BRIEF working memory subscale (as rated by both parents and teachers) and on the initiate, monitor and metacognitive index subscales (as rated by teachers). Six months following training teachers also rated a significantly greater improvement on a composite ADHD symptoms index for the CWMT group compared with the control group.

Objective measures

A study by Green et al. (25) demonstrated reduced symptoms of inattention using an observational design comparing behaviour during an academic-type task in children who trained on the adaptive CWMT with children who trained with the non-adaptive control condition. Following the intervention period, the observers, who were blind to group belonging of each individual participants, rated those who had trained with CWMT as significantly less inattentive compared with the control group. Furthermore, the study by Bigorra et al. (72) reported significantly greater improvements in accuracy for both targets and non-targets (detectability) on the Conners' continuous performance test for the group that trained compared to controls, indicating improvements in sustained attention.

It is important to note that Cogmed does not claim to be a treatment for ADHD, rather Cogmed can be a useful tool to help with some of the symptoms commonly present in ADHD. More research is currently needed to be able to more precisely predict which patients will notice significant improvements in their symptoms. However, the current research literature combined with years of clinical experiences suggest some factors that might influence training success to be co-morbidity, and the degree to which WM deficits influence the ADHD symptoms. For example, two studies that did not find significant effects included samples of ADHD with high co-morbidity. In the case of Chacko et al. (32) a large proportion of participants had co-morbid diagnosis of ODD. Meanwhile the study by Gray and colleagues (27) recruited all participants from a semi-residental school with the following inclusion criteria "coexisting LD/ADHD previously diagnosed in the community, plus severe problems in learning and behavior as well as poor response to the available standards of care and intervention" (27, page 2). Including a high proportion of (or exclusively) participants with co-morbidity make these results difficult to interpret with regards to effects specific to ADHD as any effects observed might be diluted or exaggerated due to the additional diagnoses, and thus these results cannot be generalized to ADHD as one category. It may be noteworthy that even in this heterogeneous and difficult to treat sample, there was a significant relation between the improvements on the WM tasks (index improvement) and the reduction on symptoms rated by parents on inattention and hyperactivity (IOWA Conners rating scale), however, not evident at the group level. These studies could be considered to test the boundaries of the Cogmed method and cannot be considered to inform of the efficacy of CWMT in ADHD in general. More studies are required to address for whom CWMT will lead to relevant improvements and under which conditions training should be performed.

Claim 6

Research studies of CWMT report improved cognitive functioning in daily life (28, 47, 71, M3, M5)

There are a number of studies in adults that have reported training related reductions on frequency of self-rated cognitive failures (Cognitive Failure Questionnaire). This has been shown in healthy aging (28), adults with ADHD and learning difficulties (47, 49), with Mild Cognitive Impairment (71) and in patients with acquired brain injury (5, 15, see Claim 7 specifically). For studies including a follow-up measurement, effects were evident also 2 to 6 months after CWMT (15, 28, 37, 38, 47). Effects after CWMT on functioning in everyday life have been summarized in two meta-analyses and both of these have found reliable improvements (M3, M5). One of them analysed the sustainability of the effects and found that about 90% of the effects were maintained at least 2-8 months post intervention (M3). Together this points to improvements in daily functioning that are related to CWMT and that these improvements are of the magnitude that they are noticed by the trainees themselves.

Claim 7

Adults with acquired brain injury report reductions of symptoms after CWMT in clinical trials (5, 15, 37, 38)

Impairments in WM capacity are common in patients with acquired brain injury and these patients often report on related everyday problems such as problems with their focused and divided attention, difficulties with multitasking and impaired flexibility to switch between strategies. This has motivated a number of clinical trials investigating the effects of CWMT in patients in the post-acute phase of acquired brain injury (>1 year since injury occurred). These studies have demonstrated that patients, with observed WM deficits, improve their WM capacity following CWMT. In addition, patients in a number of studies have reported transfer of these effects to everyday functioning, as measured with the Cognitive Failure Questionnaire (5), the Barrow Neurological Institute Screen for Higher Cerebral Functions (38), and the Fatigue Impact Scale (37 based on the same sample as 38) and self-rated general health after 6 months (15). Furthermore, two studies (5 & 15) have demonstrated improvements on the Paced Auditory Serial Addition Task (PASAT), which in addition to WM also place a high demand on attention and arithmetic skills. The majority of patients included in these studies were suffering from brain injury as a result of a stroke, but others from causes such as traumatic brain injury, encephalitis, and tumour. A large meta-analysis with a specific clinical focus on effects of WM training concluded that CWMT reduced disease-related symptoms in patients with WM deficits and that these results were stable over time (M5). They also state that:

> “Patients with acquired brain injuries benefited strongly from the intervention that was shown by an increased WM performance immediately and at follow-up after several months.” (Weicker et al., 2015, p. 14)

Claim 8

Improvements on measures of cognitive control have been demonstrated in studies after CWMT (1, 3, 41, 72, M5)

WM is one of the key functions that interacts with other so called “executive functions” and performance on WM tasks often correlate with performance on tasks requiring a top down control of the selection of a response, i.e. cognitive control (also referred to as response inhibition). It has therefore been assumed that improving WM capacity could possibly transfer and improve cognitive control. This has been investigated in a number of trials and also been demonstrated with for instance effects on the Stroop task (1, 3). The Stroop task measures the ability to efficiently ignore interfering information in order to respond accurately and quickly. A similar construct is assessed with the Head Toes Knees Shoulders test for pre-school children where the child has to do the opposite motion of what the examiner shows (e.g. touching toes when the examiners touches their head). One study on 4-6-year old children with “at risk” classroom behavior showed a large improvement on this task three months after CWMT compared to the control group (41). There are also measures available from tasks assessing sustained attention that rely on cognitive control or inhibition, e.g. the number of commission errors performed during a continuous performance task (CPT) would be the number of times a response was made when it should have been ignored. Effects on such a measure has been demonstrated in a RCT on children with ADHD (72). While other studies have also seen (medium to large) effects on similar tasks (Stroop or Go/no-go), they have sometimes been underpowered to reach statistical significance (18, 42, 78). When summarising the effects from all populations studied in trials assessing CWMT in a meta-analysis, there seems to be a small general effect on cognitive control (M5).

Pearson

General discussion

The interest in cognitive training has increased drastically over the last few years, as evident both in the number of research papers being published and the media attention it receives. As the field is expanding we are learning more about the mechanisms behind training, but there is still a lot to learn. It has now been shown in many meta-analyses that the type of intervention matters for outcome and Cogmed has repeatedly been shown to lead to larger improvements on WM than do other interventions (M1, M5, M6). This highlights the fact that the type of intervention that is used matters a great deal, something that might seem obvious but that has largely been ignored in much of the discussions regarding "brain training". It shows that Cogmed stands out and should not be lumped together with other brain training programs. There is also an increasing knowledge of the importance of implementation of the training, that is, it is not only important which type of training is being done but also *how* this is done, which is discussed in more detail below under "Implementation quality".

An area that still needs more research is that of the variability in improvements observed both between individuals and between studies. Any one study is prone to errors of different kinds, for example those of Type I and II statistical errors as described in the introduction. Other issues leading to problems with interpreting the results can arise from study design and execution, for example quality of the implementation and of the measures used. Another important aspect is to consider the control group used and what this actually controls for. Typically the inclusion of a control group stems from a wish to equalize all factors but the active ingredient between the groups. The factors most commonly discussed in the literature include controlling for test-retest improvements (improvements due to taking a test a second time), expectation/Hawthorne effects (increases in task performance or ratings because of the expected benefits of the participants and the additional attention received from being in a study) and the type of control condition (active vs. passive) used, which in the active condition would control for the time spent doing an activity out of the regular routine. Many studies have used the non-adaptive version of Cogmed in their designs which has made it possible to control for all of the above listed factors. However, the Cogmed non-adaptive training protocol is a control in which the final contrast being analysed consists merely of the effects from the adaptivity of the algorithm, thus both conditions would contain part of the "active ingredient". It is quite possible that this therefore should be considered an analyses of training dosage effects rather than a comparison between training and placebo. This is probably of specific concern in studies of low performing individuals, such as young children, and in studies where the non-adaptive level is set relatively high. Some studies with participants as young as 5 years of age have used a non-adaptive training set at level 2. Although this might sound low at first glance one should consider that it is not uncommon that children this age have a capacity of 3-4 items, meaning that participants in this control condition at level 2 would be performing trials at 50% or higher of their capacity. Therefore it is quite possible that also the non-adaptive training will lead to some training effects, thus diluting any effects when this is contrasted to the adaptive training group.

Due to the risk of results from any one study to be influenced by any of these errors it is important to not draw any strong conclusions from one single study. It is with this in mind Cogmed has set the criteria for claims as described above. Cogmed also continuously follows new research being published on Cogmed and as a result, continues to update the claims according to the data.

Implementation quality

One important factor that could, and most likely is influencing the results from different studies of Cogmed interventions is the quality of the implementation. This in turn depends on a number of aspects for instance; how motivated the trainees are, the degree of involvement by the coach and the effects of that involvement, the conditions under which training took place (school/clinic/home/busy/quiet environment) and the intensity of the load placed on WM during the training. While some of these aspects are difficult to quantify, this latter point is possible to measure. One of the theoretically likely (and empirically demonstrated in Klingberg et al (2005) for instance) key factors to improving WM is the constant pushing of capacity boundaries. This is established in CWMT by using an adaptive algorithm that adjusts and challenges the trainee at a level where he/she can successfully reproduce about every other trial. However, if the trainee chooses to, he/she can refrain from working at this level and work at levels below their capacity. This type of WM training is shown to be less efficacious than training pushing the limits of capacity (3, 22) and in practice would mimic training with the non-adaptive protocol (below the capacity limits). Cogmed R&D has developed a way to track the degree to which training is performed close to the trainee's capacity limit. This is called "effort score" and is the share of trials performed within approximately one level below the max level successfully reached up to this point in the training (this is constantly adapted). The effort score has been shown to correlate moderately with self-rated motivation using the Intrinsic Motivation Inventory. This tracking system was released to the first account as a coaching tool in version 4.1 of Cogmed (April, 2015) to aid in large-scale implementations. It is called "Trends" as it gives a snapshot of the quality of an ongoing implementation. Hopefully, this type of metric can offer a way for researchers to control for the degree to which training is performed close to the capacity limits in analyses of individual training effects.

Claims that Cogmed does not make

Since the usability and evidence base for Cogmed is often misstated in media and even in some academic research papers, it is also important to clarify some common misconceptions about the effects or intended use of Cogmed. Below are some examples:

- Cogmed is not a treatment for ADHD, but can help reduce some of the symptoms commonly present in ADHD that are related to poor WM function.
- Cogmed does not replace formal education, but should rather be seen as an add on that can potentially aid learning in an educational setting. Therefore, if Cogmed is used within a school setting it is important to plan the implementation to interfere as little as possible with formal teaching.
- Cogmed is not a magic pill and assigning someone to a Cogmed training does not automatically improve his or her WM. Compare this

with physical exercise for which it is not sufficient to just go to the gym, but in order to gain strength you have to put in effort and hard work. The same is true for Cogmed and although this is acknowledged in practice and reflected in the elaborate coaching system that is a crucial part of Cogmed, this is unfortunately rarely acknowledged in the research literature. An important aspect for future research to investigate is the predictors and relations between what is observed in training performance (what is put in) and effects resulting from training (what comes out).

- Cogmed is not a cure for dementia, cognitive decline related to aging, or Alzheimer’s disease but can potentially help with working memory related problems commonly seen in these cases.
- Cogmed does not help everyone with everything, but does seem to help individuals who are hindered by their poor WM and for those individuals the benefits are more noticeable to themselves and sometimes even objectively measurable.

Conclusion

The number of research studies investigating the effects seen after completion of the CWMT program are growing each year, with more than 80 peer-reviewed publications as of March 2016. The findings that are repeatedly reported include sustained improvements on WM and attention in both children and adults. Training effects have been reported in children and adults with ADHD, children with learning difficulties, hearing impairments, low language abilities, born prematurely, with intellectual disability, in adults with acquired brain injury and in typical samples ranging from preschoolers to older adults. Improved WM capacity is in itself of immense value as it enables more efficient information processing, thus the theoretical link to daily functioning and learning is self-evident. Because formal learning is dependent on information processing in WM, it would seem obvious that better WM would lead to better learning. However, that is for empirical research studies to investigate. Such evidence is starting to emerge, even though this type of research faces many challenges. Assessing learning requires longitudinal approaches, sensitive measures and flawless research design (control groups etc.). These types of studies are both expensive and cumbersome to undertake. While CWMT is the most researched WM program

to date (both commercially and non-commercially), more studies are needed to further address more specific effects in daily life, further optimization of the method and further individualization of the training. A substantial body of evidence suggests that CWMT has valuable, relevant impact on people's lives, and with a growing interest in the method one can anticipate an elevating knowledge base to help impact lives even further. Cogmed has always been and continues to be dedicated to Always Learning.

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