# Can PC-based training boost working memory in ADHD preadolescents on medication?

A clinical intervention study

Kjell Tore Hovik



Thesis submitted to The Professional Program in Clinical Psychology

> Department of Psychology UNIVERSITY OF OSLO Autumn 2010

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# ABSTRACT

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**Title:** Can PC-based training boost working memory in ADHD preadolescents on medication?

#### Supervisor: Jens Egeland

**Background:** Children with ADHD suffer from impairments in working memory, and recent studies have documented significant gains in working memory (WM) in children diagnosed with ADHD after participating in a PC-based WM training program. Earlier studies have focused on unmedicated children, while a majority of Norwegian children diagnosed with ADHD take ADHD medication for the disorder. The main question addressed in this study is whether ADHD children on medication would also show significant improvements in WM after PC-based WM training. A second issue examined is whether the results favor one of two established, but diverging, non-unitary models of the construct *working memory*.

**Method:** Sixty-six children diagnosed with F90.0 Hyperkinetic disorder (ICD-10) currently receiving treatment in the child psychiatric services in two Norwegian counties were invited to participate. Participants were randomized into treatment and control groups. The treatment group underwent a 25-day training program; controls received treatment-as-usual. Data from the forty-four children in the study who were on ADHD medication is the basis for the study.

**Results:** All subjects in the treatment group completed program requirements and showed significant gains on training tasks. The post-intervention testing showed a differential improvement in the treatment group on visual and verbal forward condition tasks, but no significant differential improvement on reverse order tasks; nor on two divided attention tasks.

**Conclusion:** The results indicate that ADHD children on medication can improve on neuropsychological measures of verbal and visuospatial short-term memory by training systematically on computerized working memory tasks; the same gains on more complex verbal and visuospatial WM tasks were not registered in the current study. Investigations into possible transfer effects of the short-term memory gains to math and reading abilities, and the long-term effects of the training on functioning at home and at school will be needed before any conclusions or recommendations can be made about the benefits of the training program.

# ACKNOWLEDGEMENTS

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My sincerest appreciation also goes to all the parents, teachers and children in the study who committed to a strenuous journey with an uncertain outcome. Although there have been earlier attempts to carry out this kind of cognitive training study for ADHD youth in Norway, this is the only major experimental WM training study to my knowledge that has succeeded through to completion. It is a testament to the tremendous energy invested by everyone involved in the study, and particularly the staff at the Vestfold Mental Health Care Trust, Department of Research, that every single child in both treatment and control groups who completed the pretesting phase carried through to Post-test1. Exhausted, but with a smile on their face.

Kjell Tore Hovik Oslo, October 2010

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# INTRODUCTION

A glimmer of hope or a chimera of exaggerated promise. The future can be daunting for families with a child diagnosed with ADHD. Statistically, children diagnosed with ADHD have a higher risk of substance abuse and antisocial disorders and generally lower educational and vocational outcomes (Mannuzza, Klein, Bessler, Malloy & Hynes, 1997). The disorder is also highly heritable, so children with ADHD are quite likely to have one or more parents suffering from the same behavioral difficulties as themselves (Barkley, Fischer, Smallish & Fletcher, 2006; Gillis, Gilger, Pennington & DeFries, 1992). On the other hand, the symptoms that can lead ADHD sufferers into challenging life situations are often precisely the qualities that lift some to tremendous heights of achievement in sports, business, politics and art. Despite numerous success stories, however, most families with children exhibiting symptoms of ADHD face a lifelong struggle with an uncertain future. The families and children need tools to help them make the best of an uncertain future, and there is a pressing need for effective interventions that can inspire hope -- not false expectations, but realistic prospects based on empirically grounded clinical evidence.

## Aim and scope

The aim of the current study is to assess whether computerized cognitive training can boost working memory capacity in ADHD-diagnosed children on ADHD medication. An additional objective is to investigate whether the results can contribute to the debate about the contents of the theoretical construct *working memory (WM)*.

Various theoretical and practical constrains have necessitated limiting the scope of the paper. First, the overall clinical study invited all children aged 10 or 11 years (+/- 3 months) diagnosed with ADHD and in treatment by the specialist child psychiatric services in Vestfold and Telemark counties to participate in the training program. Although a total of 66 children met the inclusion criteria and were included in the overall study, only results from the 44 children stabilized on ADHD medication will be included in this paper. The reason for this decision is that a majority of children diagnosed with ADHD and in treatment by the specialist child psychiatric services in Norway are on ADHD medication, and no cognitive training studies have previously focused exclusively on this group. The second limitation is that while the overall study included a wide range of neuropsychological tests, a host of behavior rating scales (self-report by parents and teachers) and a series of math and reading tests, the scope of the paper will be limited to the neuropsychological measures assessing the cognitive construct *working memory (WM)*, as later defined in this paper. Third, the overall project design calls for a pre-test, a training period, a post-test1 (two weeks after completion of the training period), and a follow-up post-test2 (seven months subsequent to post-test1). Due to unforeseen delays, Post-test2 will not be completed until early 2011. The current paper will therefore focus exclusively on pre-test and post-test1 results.

### ADHD and ADHD medication

The combination of inattentive, hyperactive, and impulsive behavior in children is recognized as a disorder when these behaviors are severe, age-inappropriate and impair functioning at home and school (Swanson, Sergeant, Taylor, Sonuga-Barke, Jensen & Cantwell, 1998). Two separate terms, attention-deficit hyperactivity disorder (ADHD) and hyperkinetic disorder (HKD), are used to describe the disorder internationally, and belong to two separate diagnostic systems, Diagnostic and statistical manual of mental disorders (DSM) (American Psychiatric Association, 2000) and the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) (World Health Organization, 1992), respectively. Although DSM is more flexible and allows for the subdivision of individual symptom clusters into individual diagnoses, few differences in identifying children meeting the full criteria set in both systems have been found in comparison studies examining neurodevelopmental, academic and cognitive functioning (Tripp, 1999). Even though the formal diagnosis ascribed to all of the participants in the current study is F90 Hyperkinetic disorder (ICD-10), the more common term ADHD will be used throughout this paper to refer to the diagnostic category and the medication prescribed to relieve accompanying symptoms.

International epidemiological studies have shown the worldwide prevalence rate for ADHD in the general population to be approximately 3-6% (Farone, Sergeant, Gillberg, & Biederman, 2003; Polanczyk, Silva de Lima, Horta, Biederman, Rohde, 2007). While a smaller number of children are actually diagnosed for the condition, a large number of children in Norway who receive the diagnosis take medication for the condition. The exact number of children with an ADHD diagnosis in the age-group 10-12 years in Norway and the number of children on ADHD medication is not known. However, an indication of the scope of the disorder from a

public health perspective is that approx. 27% of the children (7671 children) receiving a diagnosis in the specialist psychiatric health services for children in Norway in 2005 were diagnosed and treated for Hyperkinetic disorder (F90) (Bronder, 2010). There are signs that the use of medication to treat the disorder is on the rise. In a Norwegian study, the use of medication for children between 10-13 years was investigated for the period 1999-2004, showing that the number of children receiving medication increased two and a half fold during that same period (Åsheim, Nilsen, Johansen & Furu, 2007). The authors report in the same article that this trend is consistent with developments in the rest of the country.

Even though an ADHD diagnosis cannot be made based on the basis of neuropsychological tests alone, impaired cognitive performance has been linked to children diagnosed with ADHD independent of family history and comorbidity (Seidman, et al., 1995). Cognitive deficits as measured by neuropsychological tests have been shown in a Norwegian population of children as well (Lundervold & Sørensen, 2008). In the current study, all participants underwent a comprehensive clinical assessment and were diagnosed with F90 Hyperkinetic disorder (ICD-10 criteria) by a team consisting of a specialist psychiatrist, a psychologist, a clinical therapist and a clinical social worker employed in the specialist health services units either in Vestfold or Skien counties and had been stabilized on an ADHD medication in advance of their participation in the study.

The goal of ADHD medication is to reduce symptom severity and improve everyday functioning. A Norwegian researcher on ADHD, Pål Zeiner, maintains in his book that approximately 75% of children diagnosed with ADHD in Norway experience a reduction in symptoms after starting on medication (Zeiner, 2004). Medication is, however, a controversial topic, with opponents often aggressively opposed (for the debate in Norway, see Idås & Våpenstad, 2009). Several studies investigating possible mechanisms underlying the disorder have shown that ADHD is characterized by a dysfunction in dopaminergic transmission in the frontal lobes and in striatal (basal ganglia) structures (Vaidya et al., 1998). Dopaminergic dysfunction is suspected in ADHD because symptoms respond favorably to stimulant medication that release and inhibit reuptake of catecholamines, particularly those with a modulatory influence in frontal-striatal regions. Dysfunction in frontal-striatal-cerebellar circuits are thought to be responsible for cognitive deficits such as inhibition, delay aversion and executive functioning (Krain & Castellanos, 2006). Functional imaging studies have shown reduced metabolism in fronto-striatal and striatal regions in ADHD (Castellanos et al.,

2002), and SPECT studies have shown markedly decreased activity in the prefrontal cortices of brains of ADHD adolescents at rest compared to healthy controls (Amen & Carmichael, 1997). Although medication is often an important part of the treatment for the disorder, according to a guide for health practitioners issued by the Ministry of Health and Care Services (2005), medication must only be prescribed to persons diagnosed with ADHD in combination with psychosocial and/or special education measures. A landmark study in the USA comparing the use of medication and therapeutic interventions, the Collaborative Multisite Multimodal Treatment Study of Children With Attention-Deficit/Hyperactivity Disorder (MTA), found that while ADHD medicine is an essential part of treating ADHD, the best combination for many children was combining medication with other treatment (Molina et al., 2009). Whatever the benefits of using medication for ADHD may be, the effect lasts only as long as the person is taking the medicine, while behavioral or cognitive interventions have the potential for long-term change (Mikkelsen & Thomsen, 2005). From a clinical perspective, the urgency in providing children with beneficial treatment options lies in the chance of enabling a favorable behavioral and cognitive developmental path to emerge as early as possible.

The most common medicines used in Norway to treat ADHD are Ritalin, Concerta, Equasym and Strattera. Of the 44 children included in the study, 14 were on Ritalin, 18 were on Concerta, seven were on Equasym and five were on Strattera. The active ingredient in the first three preparations is methylphenidate, which is a stimulant medication that releases and inhibits reuptake of catecholamines -- particularly dopamine which has a modulatory influence in frontal-striatal regions (Vaidya et al., 1998). The three brands differ in terms of the duration of the effect. The active ingredient in Strattera is atomoxetine, which is not a stimulant, but by inhibiting the reuptake of norepinephrine has been shown to improve inhibitory control (Chamberlain, et al., 2007). In this paper, reference to the first three brands mentioned above will be referred to as "stimulant medication", while reference to all four brands will be referred to as "ADHD medication."

A 2008 meta-analysis of 24 RCT studies investigating the effects of methylphenidate and psychosocial treatments either alone or in combination found that while methylphenidate and psychosocial treatments (e.g. parent management training) reduced ADHD symptoms, there was no substantial improvement in academic function (Van der Oord et al., 2008). A U.K. report in 2006 comparing the effectiveness and cost-effectiveness of various ADHD drugs

such as methylphenidate and atomoxetine concluded that drug therapy seemed to be superior to no drug therapy at all for the children taking the drugs, but that there was no evidence that there were any significant differences between the drugs in terms of efficacy or side effects (King et al., 2006). However, researchers have found specific cognitive benefits to working memory from the use of methylphenidate (Bedard, Martinussen, Ickowicz, & Tannock, 2004; Elliott et al., 1997; Mehta et al., 2000). These researchers argue that it is the increase in the transmitter substances dopamine and norepinephrine that enhances working memory function. Some researchers report having pinpointed working memory deficits to D<sub>1</sub> receptor cells and have shown amelioration by targeted stimulation treatments (Goldman-Rakic, Castner, Svensson, Siever, & Williams, 2004). While stimulant medication has been shown to improve visuospatial WM with effect sizes of approximately 0.5 (Barnett et al., 2001), 0.4 to 1.2 (Bedard et al., 2004), and 0.4 to 0.7 (Kempton et al., 1999), PC-based WM training in unmedicated children has been shown to increase WM function by an effect size of 0.93 (Klingberg et al., 2005).

In conclusion, there does not seem to be a consensus on the specific effects of ADHD medication in general on cognitive performance, perhaps because the medication is targeted toward the more general behavioral symptoms of ADHD and not at specific cognitive deficits. There does, however, seem to be evidence that ADHD medication may have a positive effect on WM performance, although the amount of gain is less than the reported gains from computerized WM training in unmedicated children. In any event, there is agreement that medication alone is not sufficient to treat children diagnosed with ADHD.

### Preadolescence

Preadolescence is a sensitive transition period from childhood to young adulthood during the ages of 10-12 years. It is a period of growing self-identity, self-awareness and independence, but not yet with the demands and pressures of adolescence. At the end of this developmental period, children in Norway move from the elementary school level to middle school, which involves higher academic demands and pressures. This is also an age when a majority of children with ADHD are first diagnosed with the disorder and come into contact with the specialist child psychiatric services in Norway. Screening and diagnosing the disorder at an early age has been shown to be counterproductive unless followed up by effective intervention options (Sayal et al. 2010). Although all of the children in the current study have

been diagnosed with ADHD and receive medication for the disorder, only 61% of the children were receiving special education at school for their cognitive difficulties at the time of inclusion into the study.

A study from the field of anthropology supports the case that preadolescence might be an ideal age-group for a clinical training intervention designed to influence developing minds . A study of Japanese children growing up in the United States found that children were particularly sensitive to the incorporation of cultural meaning systems, including affect, cognition and behavioral patterns between the ages of 9 and 15 (Minoura, 1992). The author of the study does not link this sensitivity directly to emerging neuropsychological capacities, but data from the study clearly documented that the preadolescents adopted the cognitive and behavioral patterns they were exposed to during precisely these years and retained the patterns into adulthood regardless of the cultural exposure before and/or after that period. A training regime aimed at molding favorable cognitive processing patterns at this impressionable age could potentially have a tremendously positive effect on the cognitive development of the child. Another field of investigation also supports the idea of possible dramatic benefits arising from systematic, intensive training of fundamental cognitive processes, namely the treatment of dyslectics. A training intervention study published in 1991 involving a group of severe dyslectics averaging 10 years of age showed that intensive training in analytic decoding for an average of 65 hours resulted in significant improvements in reading comprehension. The intervention was not computerized, nor were all of the children able to convert the training in phonological awareness to reading proficiency; nevertheless, for the majority of subjects in the sample, cracking the code of reading through intensive, systematic training opened up tremendous, new capacities and horizons.

The major finding in numerous studies strongly suggests that children with ADHD are at a significantly higher risk of dropping out of school and growing up into adulthood marked by antisocial and substance-related disorders (Mannuzza, Klein, Bessler, Malloy & LaPadula, 1998). A problematic negative trajectory for these children is often laid out in the preadolescent years. An effective early intervention to lift the child cognitively at precisely this sensitive period in their lives and mental development would be an important tool for health professionals working to better the odds of success for this vulnerable group.

### Mechanisms of change

The continuous repetition of specific cognitive processes in a systematic fashion can reasonably and intuitively be expected to have an enabling effect on that cognitive process, either by making the neurological substrates underlying the process better organized and more efficient, or by affecting the process through learning in a way that makes the cognitive process more generalizable to a wider range of processes. The old adage, "practice makes perfect", once reserved for the domain of sports, is now increasingly being recognized in the cognitive sciences as a genuine adaptive property of the brain, and the advent of imaging technology is helping document the malleability of cognitive structures and processes. Although the change mechanism is by no means fully understood, the scientific community is now open to the possibility of being able to enhance cognitive performance through training. In the current paper, two principles of change by experience, *neuroplasticity* and *far transfer*, are proposed as change mechanisms that could help to explain how a systematic training program could permanently alter a cognitive process.

#### Neuroplasticity

Neuroplasticity and neurogenesis refers to the brain's ability to adapt and change (Gould, Reeves, Graziano, & Gross, 1999), and recent years' investigations using anatomic and functional brain imaging techniques are shedding light on the long-running debate in the cognitive sciences on the possibility of neuronal change and development throughout an individual's lifespan. Although brain size is approximately 90% of its adult size by the age of six, grey and white matter in the brain continues to undergo dynamic changes throughout adolescence (Casey, Galvan, & Hare, 2005). Among the findings relevant to the current study, researchers have correlated maturational change in the prefrontal structures of adolescents with neuropsychological performance measures (Sowell, Delis, Stiles, & Jernigan, 2001). Prefrontal structures are at the heart of executive functions that mediate important regulatory functions such as inhibition, attention and WM. White matter development is related to myelination of axons, and the development of white matter is paralleled by the development of cognitive functions. A study published by the Klingberg group has shown regional and functional specificity of this maturation (Nagy, Westerberg, & Klingberg, 2004). Specifically, the authors found that improvement in WM were associated with increased anisotropy in the superior and inferior parts of the left frontal lobe, i.e. enhanced directional flow through brain tissue. Another study by the same group found increased prefrontal and parietal activity after WM training (Olesen, Westerberg, & Klingberg, 2004).

Neuronal change processes are not the exclusive domain of children, however. Researchers publishing an article in Nature in 2004 reported findings of relative grey matter change in adults after a systematic 3-month juggling program (Draganski et al, 2004), and neuronal plasticity has been shown in adult musicians (Münte, Altenmüller, & Jäncke, 2002). In fact a large body of fMRI evidence has been amassed showing the dynamic reorganization of neural substrates in the cortex as a result of weeks of training (Ungerleider, Doyon, & Karni, 2002). These findings seem to indicate that, maturational changes aside, systematic training can potentially induce neuronal changes in the brain independent of maturational processes.

#### **Far Transfer**

While neuroplasticity refers to the physical adaptability of cognitive structures, Far transfer refers to the functional transfer of learning from one training context to another. In cognitive terms, the concept is related to the distinction between crystallized and fluid intelligence, in which the former refers to a general achievement factor involving the ability to use learned skills, knowledge and experience, while the latter is a more basic general intelligence capacity involving the ability to think logically and solve problems in novel situations independent of acquired knowledge (Catell, 1963). Within the exclusive domain of skill learning, certain types of learned skills may only have relevance to the specific task trained, while other types of learning have pervasive and enduring effects on the mind and foster generalized thinking patterns that go beyond the specific training tasks provided (Barnett & Ceci, 2002). The discussion about how best to generalize knowledge to multiple domains has been ongoing since the time of Plato, but there is still no clear, agreed upon definition of what "carrying over" or "a new context" constitutes (Barnett & Ceci, 2002). Some researchers have found evidence of transfer gains after computerized WM training (Holmes, Gathercole, & Dunning, 2009; Klingberg, Forssberg, & Westerberg, 2002; Klingberg et al., 2005). The children undergoing the intervention in the current study train on tasks thought to boost a cognitive process believed to underlie a multiple range of everyday cognitive processes, such as mathematics and reading. While WM training studies have shown spill-over gains to areas such as math and reading abilities, the current paper will focus on the ability to transfer gains

achieved by training on specific tasks on a computer to similar, but non-trained neuropsychological tests. Perhaps not a leap of faith, but an important leap, nonetheless.

In summary, although neuronal change and change processes are not fully understood, the indications are that training can influence neuronal development and functions independent of genetic and maturational factors. And even though a taxonomy of learning transfer has yet to be accurately described (Barnett & Ceci, 2002), we all share an intuitive understanding that learning in a specific area and on a specific task can generalize into other areas and onto other tasks if systematically and appropriately acquired. This window of potential to help young, forming minds is precisely the opportunity a systematic WM training program is designed to address.

## Working memory

The tremendous interest in the concept of WM is largely owing to the fact that many researchers believe it may be the single most important factor in determining general intelligence (Kyllonen & Christal, 1990); others have called it the "hub" of intelligence (Haberlandt, 1997). WM is needed for a wide range of cognitive tasks that require online maintenance of information, and correlations between WM and general intelligence have been shown to be r = 0.7 depending on the WM task used (Conway, Kane, & Engle, 2003). The prospect of isolating an underlying mechanism of intelligence that could be enhanced by specific training techniques would be a holy grail for everyone working in the teaching profession. In particular, a training regime boosting WM capacity would be tremendously beneficial for large numbers of clinical groups (e.g. ADHD, schizophrenia, depression) shown to have cognitive WM impairments that mirror the behavioral challenges they face on a daily basis.

#### **Theoretical models of WM**

A great number of WM models have been launched to provide a theoretical basis for research into this cognitive function. While some established models focus on executive dysfunction (Barkley, 1997) and cognitive effort (Sergeant, 2005), others propose biophysical explanations for the disorder (Macoveau, Klingberg, & Tegner, 2006). There is, in fact, a general state of quandary about the exact contents of WM (Engle, Tuholski, Laughlin, & Conway, 1999; Miyake & Shah, 1999; Perry et al, 2001). There are often not clearly defined or operationalised boundaries between short-term memory (STM) and WM, and a host of inconsistent metaphors are in use for WM, i.e. box, workspace, blackboard, mental energy, and resources. The two established WM models chosen as an interpretive framework for the current study are described by Alloway, Gathercole & Pickering (2006) and diverge on the role of the attentional component in mediating the models' information storage and processing systems. The models have been chosen, because, while they have a similar conception of the theoretical division of storage and processing components of WM (i.e. a non-unitary framework; see Miyake & Shah, 1999), they diverge specifically on the control mechanism regulating the system. This should make them amenable to construct testing by examining whether the test results disassociate any differential effects of training on the control mechanism versus impacting on the more basic storage and processing process.

In the most established of the two models, the authors hold that WM consists of a domaingeneral feature that coordinates information coming from two separate storage components for verbal and visuospatial input. This model, originally proposed by Baddeley and Hitch (1974), and referred to as the domain-general model, features a so-called "central executive" that controls resources and monitors information processing across informational domains (Baddeley, Logie, Bressi, Della Sala, & Spinnler, 1986; see Engle, Kane, & Tuholski, 1999 for a review). Two domain-specific slave systems hold the information temporarily for processing - in the phonological loop for verbal information, and in the visuospatial sketchpad for visual and spatial representations. A fourth component of the model was added later, the episodic buffer, which is responsible for binding information across informational domains and memory subsystems into integrated chunks (Baddeley, 2000). The domaingeneral model of working memory is supported by evidence from studies of both young children (4-6 year-olds) (Alloway, Gathercole, Willis, & Adams, 2004) and adult subjects (Jonides, Lacey, & Nee, 2005). The authors Engle and colleagues (Engle, Tuholski et al., 1999) have a similar WM model that extend the original model and propose that WM is more accurately described as a passive store component, plus attentional control (Alloway et al., 2006). In the current paper, the modification will be considered under the same domaingeneral view.

The authors of the diverging view argue that WM resources are separated into two separate pools of domain-specific resources for verbal and visuospatial information (Alloway et al.,

2006; Daneman & Tardiff, 1987; Shah & Miyake, 1996). In this model, referred to as the domain-specific model, each domain is independently capable of manipulating and keeping information active. Evidence from research on adults and older children have been shown to support this model (Friedman & Miyake, 2000).

According to the domain-general account of WM, the short-term storage aspect is supported by a domain-specific component, e.g. a verbal or a visuospatial store, but the more complex, processing aspect of the task is controlled by a centralized component, e.g. the central executive or controlled attention. This means that there could be an improvement in the slave systems without an improvement in the central executive; or conversely, an improvement in the central executive without a corresponding expansion of capacity in the slave systems. In the domain-specific perspective, on the other hand, performance in complex tasks is a function of the efficiency in either verbal or visuospatial abilities; thus, performance in verbal working memory tasks would not predict spatial abilities, nor would spatial WM measures be highly associated with verbal skills (Alloway et al, 2006). Being essentially independent, the two domains should be more easily distinguishable and separable when analyzing the effects of new learning on the separate functions. One of the aims of the current study is precisely to see whether the systematic training of visuospatial STM and WM abilities in the training group will have a dissociative effect on the test results of verbal and visuospatial STM and WM tests post intervention.

#### **Distinguishing between STM and WM**

The construct *working memory* has had a long and convoluted history with researchers attributing different definitions and operationalisations down through the years. A central issue has been the relationship of WM to the concept *short-term memory* (STM), originally forwarded by Atkinson & Shiffrin (Atkinson & Shiffrin, 1971). Although there is evidence indicating that STM and WM are the same construct (Engle, 2002), researchers such as Cowan (2008) have argued that the difference is important because the more attention-demanding measures associated with WM correlate highly with aptitudes, whereas the more routine measures associated with STM do not. Some cognitive training studies operate with a wide definition of WM in which there is no differentiation between STM and WM (Klingberg et al., 2002; Klingberg et al., 2005; Westerberg, 2004), while others clearly make a distinction between the two, assigning a simpler process to STM and a more complex cognitive process

to WM (Alloway et al., 2006; Holmes, 2009; Perry et al, 2001). The neuropsychological tests used in the current study (see Table 2 for a description) have been chosen for their ability to delineate functional specificity, as reported in the neuropsychological literature (Lezak, Howieson & Loring, 2004). In the current study, the term STM will be used to refer to a simpler cognitive process that Goldman-Rakic (1996, p. 13473) refers to as keeping information "transiently in mind" during a short period of time, while the term WM will be used to refer to the more advanced process of storing <u>and</u> manipulating information over brief periods of time (Alloway et al., 2006). Although there are studies that have not found differential sensitivity between backward and forward conditions of span measures (Wilde, Strauss and Tulsky, 2004), experiments such as those conducted by Engle, Tuholski et al. (1999) did find a clear distinction between STM ("a simple storage component") and WM ("a storage component as well as an attention component") by applying forward and backward condition tasks, respectively.

An important aspect of STM and WM investigated in the current study is the separability of verbal and visuospatial capacities. Several researchers support the separability of verbal and visuospatial capacities in the context of measuring WM performance (Morey & Cowan, 2005). In a study of national curriculum tests involving children in the same age-group as in the current study, Jarvis and Gathercole (2003) found a clear dissociation between verbal and visuospatial WM systems for this age group. Kane, Hambrick, Tuholski, Wilhelm, Payne, & Engle (2004) also found similar results in their experiment, but with university-level subjects. Factor analysis conducted by the authors in the Kane et al. (2004) study found that while WM tasks largely reflected a domain-general factor, STM tasks were much more domain specific.

A number of researchers put verbal and visuospatial forward and backward span squarely in the realm of measures reliably quantifying the differential mental effort associated with STM and WM. Studying working memory in adult schizophrenic patients, Perry et al. (2001) based several experiments on the differential sensitivity of forward and backward conditions on verbal (Digit Span) and visuospatial (Visual Span) tasks. While acknowledging the ongoing debate about the content of WM, the authors recommended separating functions requiring transient, on-line storage capacity from tasks requiring more complex mental manipulation with executive-function involvement, across both verbal and visuospatial domains.

Although both WM models described in the previous section accommodate a separation between STM and WM, the relationship between STM and WM in the two theoretical models of WM diverge. In the domains-general model, changes in efficiency of the central executive and the slave systems should be separable, while in the domain-specific model an improvement in WM in one domain should apply for both simple (STM) and more complex, attention-demanding tasks (WM). Thus, the current study has the potential of being able to provide results showing the dissociability of the more immediate attentional capacity of STM and the capacity to manipulate more complex information involved in WM in the context of both verbal and visuospatial domains.

#### Earlier WM training studies

Two landmark computerized training studies involving children diagnosed with ADHD showed that WM capacity could be increased by systematic, adaptive WM training using the same PC-based training program used in the current study. In the first study involving 14 children (5 on medication), the results showed significant improvements in visuospatial WM as measured by pre and post tests of simple attention span (e.g. Span Board, forwards) and more complex manipulation of information (e.g. Span Board, backwards) (Klingberg et al., 2002). The second study involved 56 patients but included only nonmedicated children; this study also found significant improvements in visual WM (e.g. Span Board) and verbal WM (e.g. Digit Span) (Klingberg et al., 2005). The latter study also found transfer effects of the training, such as significant effects on reasoning ability, response inhibition and a decrease in parent-rated ADHD symptoms. An independent study in the U.K. using the same training program for undiagnosed schoolchildren with particularly poor WM capacity found significant enhancement of working memory function after the training period and sustained function after six-months (Holmes et al., 2009). Although none of the 42 children who participated in the U.K. study were diagnosed with ADHD, an important finding was a significant difference in test results in the group who trained using the so-called *adaptive* version of the WM training program and *non-adaptive* version. In the adaptive version, the program flexibly adjusts the level of difficulty on a trial by trial basis so the child is always working at a level that closely matches their performance, while in the non-adaptive version the progression of exercises is the same for everyone. The adaptive version of the program has been used in the current study.

#### Summary and predictions

ADHD can be a debilitating disorder, and there is a need for modern treatment options in addition to medication. While ADHD medication can relieve many symptoms of ADHD, persons diagnosed with ADHD are still likely to face a challenging future with a high risk of impaired intellectual and social functioning and low academic performance. The prospect of a 5-week high-intensity, adaptive PC-based training program during preadolescence being able to boost cognitive capacity and performance seems to be too good to be true. Several studies have already documented significant effects from training in ADHD children, but the program has not yet been clinically tested on an ADHD group on medication. One possibility is that the effects of medication will have already exhausted change potential in the WM structures. A second possibility is that additional gains could be made precisely because the medication reduces behavioral symptoms that would otherwise get in the way of the change process. A third possibility is that the transfer of learning from the computer tasks will not transfer outside of the specific learning environment. In the clinic, it would be of great value to clarify whether working memory training should be recommended as an effective intervention method in combination with medication. The preadolescent children selected for inclusion in the current study are at a sensitive stage in their academic and intellectual development, and this age coincides with the setting of their diagnosis and the start of their future coping with the disorder. There seems to be no better time for such a training intervention than precisely these preadolescent years.

The first question to be addressed is, will the children in the training group improve WM function significantly compared to the children in the control group on the same types of measures used in earlier studies to assess STM capacity and WM capacity? Extrapolating from existing PC-based training studies involving children, the prediction is that the intervention group should show a significant differential effect compared to the control group in both enhanced STM capacity and WM capacity. The second question for the study to address in order to shed light on two competing conceptualizations of WM is, will there be a uniform effect across levels of processing, i.e. in simple STM-capacity and in executive aspects of WM across both verbal and visual domains? The prediction based on the earlier findings is that there should indeed be gains both across levels and across domains.

# **METHOD**

## **Subjects**

All 10-12-year-old children (+/- 3 months) in Vestfold and Telemark counties, Norway, diagnosed with F90.0 Hyperkinetic disorder (ICD-10), satisfying inclusion criteria and in contact with specialist child psychiatric services were invited to participate in the study. All of the families (66 children) responded positively, and all these children were included and randomly assigned to a treatment or control group. One child withdrew in advance of the pretest date; of the remaining children, all completed pretest, training and post-test1. Only results from the 44 children on ADHD medication in the study will serve as the basis for the the analyses presented in this paper.

A complete WISC assessment of general intelligence was required since an important inclusion criterion was that participants had to have an IQ over 70 (WISC-III or WISC-IV). Other grounds for exclusion were comorbid neurodevelopmental disorders (i.e. autism, Tourette) or a serious psychiatric disorder (i.e. bipolar, schizophrenia). Parents and teachers were also asked to complete a series of questionnaires (Strength and Difficulties Questionnaire, Behavior Rating Inventory of Executive Function and ADHD rating scale) for each child at each testing phase.

Table 1 provides a presentation of the main measures of subject characteristics. There were no significant differences between the intervention and control groups on any of the measures. The ratio of boys to girls in the current study is 3:1, which is the same approximate gender ratio found in international epidemiological studies for ADHD (Gershon, 2002). Participants' IQ level was just under average, which is common in this type of ADHD group (Egeland, Sundberg, Andreassen & Stensli, 2006; Lundervold & Sørensen, 2008).

		Intervention group	Controls	Total	Р
Gender (M/F)		15/8	18/3	75%/25%	n.s.
		M (SD)	M (SD)	M (SD)	
Age mean (SD)		10.5 (0.6)	10.5 (0.9)	10.5 (0.7)	n.s.
Verbal IQ(SD)*		92 (10.6)	96 (11.9)	94 (11.3)	n.s.
Performance IQ(SD)*		90 (16.5)	95 (17.0)	92 (16.8)	n.s.
Full Scale IQ(SD)*		90 (12.1)	94 (12.9)	92 (12.6)	n.s.
BRIEF**	Р	69 (14.1)	65 (15.8)	67 (14.9)	n.s.
Behavioral Regul. Index (BRI)	Т	67 (16.1)	65 (14.0)	66 (15.0)	n.s.
BRIEF**	Р	72 (7.5)	70 (8.9)	71 (8.1)	n.s.
Working Memory	Т	71 (12.7)	73 (7.4)	72 (10.5)	n.s.
BRIEF**	Р	71 (8.1)	66 (8.8)	68 (8.6)	n.s.
MetaCognition Index (MI)	Т	68 (11.7)	70 (7.7)	69 (10.0)	n.s.
BRIEF**	Р	71 (9.8)	67 (11.3)	69 (10.7)	n.s.
Global Exec. Composite (GEC)	Т	69 (13.7)	71 (9.8)	70 (11.9)	n.s.

**Table 1: Demographics and clinical characteristics** 

\* Wechsler Intelligence Scale for Children (3. Edition WISC - III: Wechsler, 1974)

\*\* Pre-test parent/teacher score on The Behavioral Rating Inventory of Executive Function (BRIEF)

*P* = *Parent rating; T* = *Teacher rating* 

Parents and teachers were asked to complete the Behavior Rating Inventory of Executive Function (BRIEF) for each child in order to assess every subject's pre-test state of executive functioning. Executive functions are a collection of processes that are responsible for guiding, directing and managing cognitive, emotional, and behavioral functions, particularly during active, novel problem solving (Gioia, Isquith, & Kenworthy, 2000). The BRIEF questionnaire has been shown empirically to reliably assess executive functioning in clinical samples of children and adolescents in the US (Gioia, et. al, 2000) and in Norwegian samples (Egeland & Fallmyr, 2010). Table 1 shows relevant mean scores for the children in the current study. The BRIEF manual recommends using a T-score of 70 as a cutoff point to ensure an acceptable balance between correctly identifying children with ADHD (sensitivity) and avoiding incorrectly identifying children without the diagnosis (specificity). Even though the children are on medication, the average score for the children as assessed by both teachers and parents are generally close to the clinical cut-off point, i.e. approx. two standard deviations above the average compared to normal children. The scores on the Behavior Regulation Index (BRI) are just under the clinical cutoff point, while scores on the Metacognition index (MI) and Global Executive Composite (GEC) are right around the clinical cutoff point. Although the Working Memory score is part of the Meta-Cognition index, it is reported separately since WM is a focus of the training program; both parent and teacher evaluations report clinical-level impairment in this function for children in both the treatment and intervention groups. Overall, the figures indicate that there is room for improving impaired cognitive functioning, particularly when it comes to cognitive skills and working memory functioning.

## Design

An experimental design (see Figure 1) was chosen in which the subjects who were randomly assigned to the experiment group received cognitive training and the control group received treatment-as-usual. Children in the control group were given the opportunity to participate in the training program after completion of their post-test 2 control testing.

Training Post-test 1 Post-test 2 Exp. (as of 18.10.10) 30-40 min. (N=23)a day, 5 days a Randomly Exp. Exp. week for assigned to Pretest 25 days. (N=21) experiment (N=23)(N=44)or control group. Control Treatment Control Control as usual. (N=21)(N=18)(N=21)

Research design

Figure 1. Research design with actual number of subjects completing the various stages.

An important objective was to investigate whether cognitive training could serve as a beneficial clinical intervention option for children with ADHD. Thus, it was important that the training was practically adapted to the children's everyday lives and schedules. The training therefore took place at each child's school with a school staff member being responsible for the training sessions. Persons responsible for training the children attended a training seminar to become authorized coaches in advance of the training program, and all testing was conducted either by a test-assistant, a psychologist, an educational therapist or a neuropsychologist.

## Intervention method: PC-based WM training

Participants assigned to the experimental group trained on 13 different PC-based exercises included in a computerized WM training program developed by CogMed. The same training program has been used in a number of WM training studies in recent years in several countries (in Sweden: Klingberg et al., 2005; in the UK: Holmes, 2009; a pilot study in the US: Mezzacappa & Buckner, 2010). Several of the authors in many of the studies report remarkable gains after training e.g. in children with ADHD (Klingberg et al., 2005) and in adult neurospychological patients following strokes (Westerberg et al., 2007). Some of the authors in some of these studies (e.g. Klingberg and Westerberg) have financial interests in the company that developed and markets the program (CogMed), making it important to have independent confirmation of the results.

The training regime includes three letter span tasks (all forward condition), three digit span tasks (one forward condition, two backward conditions), and seven visuospatial tasks (all forward sequenced), including static visuospatial tasks (one 2D visuospatial task, one 3D visuospatial task), and two dynamic visuospatial tasks, in which students recall the positions of rotated or moving objects. Nine of the tasks are presented purely in visual format, and four are delivered with an auditive input. Eleven of the tasks are forward sequenced, while only two are reverse order tasks. A critical feature of the program is adaptivity, i.e. the level of difficulty is adjusted continuously throughout the training program to the individual student's skill level, in the tradition of Vygotsky proximal development principles (Vygotsky, 1934/1986). Students completed 10-15 trials of eight exercises each day for a total of 115 WM trials per day. Training time averaged about 30-40 minutes per day, depending on the exercise set and the student's performance level.

### **Outcome measures**

The tests used in the current study to measure the effects of computerized WM training were chosen based on the theoretical assumptions of a separability between STM and WM (Perry et al., 2001) and their use in earlier studies to identify changes in WM functioning after training (Holmes, 2009; Klingberg et al., 2002 & 2005). Another important consideration was the test's ability to distinguish between both verbal and auditive modalities in STM and WM (see Table 2.).

	Auditive	Visual
Short-term	Digits Forward, total*	Visual span, forward**
Memory	Digit span: longest span*	
Working	Digits Backward, total*	Visual span, backward**
Memory	Digit span: longest span*	
	Letter Number sequencing*	Trail Making Test, IV***

Table 2. Summary of Measures - modality and cognitive function

\* Wechsler Intelligence Scale for Children -IV edition

\*\*Leiter International Performance Scale - Revised.

\*\*\*D-Kefs Trail Making Test IV (Number-Letter Switching)

Digit Span is a common neuropsychological test in the WISC-IV battery used to assess immediate verbal recall. The test involves a forward and a backward condition, which have been shown to involve different mental activities (Banken, 1985; Costa, 1975), in that they are affected differently by brain damage (Black, 1986). Digits Forward involves repeating a sequence of numbers right after they have been read aloud, and Digits Backward involves repeating the numbers in reverse order. Digits Forward is considered to be a good measure of attention span (Lezak et al., 2004), and it will be used in this study to operationalise the shortterm memory function in WM. Digits Backward requires the temporary holding of information presented verbally while juggling them around mentally in an effortful activity (Banken, 1985; Black, 1986); this task has been chosen to operationalise the more mentally challenging and verbally presented WM function in this study. In healthy subjects, the raw score differences between Digits Forward and Digits Backward have proven to be quite predictable (e.g., WISC-III shows a 2-digit difference on average in favor of the Digits Forward condition, Wechsler, 1991). The stable 2-digit difference in healthy subjects is also an expression of the added difficulty involved in the reverse order condition compared to the forward condition.

The Leiter international Performance Scale-Revised (Leiter–R) is a proven cognitive assessment tool that has a unique response format which is expressively nonverbal. Two tests from this battery have been chosen to measure different aspects of immediate attention span and the more challenging WM: Forward Memory: The Remembering Game (Visual span, forward), and Reverse Memory: The Backwards Game (Visual span, backward), respectively. In both tasks the stimuli to be remembered are visual images of familiar items (e.g. a frog, a

ship, a shoe). The forward condition subtest measures sequential memory span and requires sustained attention and an organized processing style. The reverse memory task is a more complex mental activity requiring the child to store and juggle information using mental effort that requires good working memory (Roid & Miller, 1997). Similarly to Digits Forward and Digits Backwards described above, these non-verbal, visual tests will be used in this study to help identify any dissociation between the simpler STM of immediate attention versus the more complex, mental manipulation requirements of WM.

In the Letter-Number Sequencing task, a list of randomized numbers and letters of increasing lengths are read aloud. Subjects are asked to repeat the numbers and letters from the lowest in each series, with numbers always coming first. Scores obtained from healthy young adults have been shown to correlate with performance on Digits Forward and Backward (Crowe, 2000). Many patients with mental disorders have normal immediate memory spans, however, and a longer and more complex span can be more sensitive to attentional deficits. Schizophrenia patients, for example have been shown to be impaired in the Letter-Number Sequencing task (Gold, Carpenter, Randolph, Goldberg & Winberger, 1997), and these deficits have been attributed to an impaired auditory working memory system that is dependent on frontal, executive system functioning (Perry et al., 2001). In the current study, the test will be used as an additional, more highly demanding measure of verbal WM.

The Trail Making Test (TMT), Condition IV, is a test of scanning and visuo-motor tracking, divided attention and cognitive flexibility (Lezak et al., 2004). The test, also called Number-Letter Switching, involves connecting circles with a pen or pencil trace and alternating between number and letter sequences. ADHD patients have been shown to have reduced frontal function, and this specific test has been linked to frontal activation (Stuss, Bisschop, Alexander, Levine, Katz, & Izukawa, 2001). Egeland (2010) found that TMT-IV was the most sensitive of a range of neuropsychological tests in ADHD subjects. The ability to engage in this type of cognitive flexibility is considered a classic executive function, and is considered essential for higher-level skills such as multitasking, simultaneous processing and divided attention (Delis, Kaplan, & Kramer, 2001). Due to the dual-task processing requirements of this task – requiring the subject to keep both the alphabet and number systems on-line simultaneously, it will be used as an operationalisation of the executive element of WM in the current study.

All computer analyses in the current study were conducted using the statistics program SPSS (version 16).

## **Practical challenges**

The overall project involved some 66 children, 132 parents, 32 teachers or school assistants at 32 different schools, 5 testing personnel and 3 administrative personnel. All of these critical contributors were engaged intensively throughout the pretest, training and post-test1 period lasting some 9 weeks, and again mobilized after 6-7 months for posttest 2 testing and filling-out of questionnaires, etc. Total involvement would span a period of some 8-9 months, and even longer for many, because control children were then followed up an additional 6-7 weeks for their post-study training. The study was an enormous undertaking that served up one obstacle after another along the way.

A major challenge was the sheer logistics involved in testing, training and following up such a large number of patients living in some 10 different municipalities and school districts over such a long period of time. Many parents, some of them presumably also suffering from ADHD symptoms themselves, had problems remembering appointments and agreements, which warranted creative and flexible solutions by the staff at the clinics on a regular basis to get the children trained and tested on schedule. Another serious challenge was the swine flu epidemic that swept through the region in the middle of the training period (autumn 2009), causing a delay of up to a week of training for some subjects. Delays meant that the child had to put in extra training days to meet minimum training requirements, and for a few of the children the additional training days fell on Christmas Eve and Christmas Day. Motivating the children and parents to complete the minimum requirements is a study in psychological persuasion techniques in itself. Another challenge was teachers calling in sick. In some cases parents had to be recruited on the spot to follow up their child's training program to ensure training compliance. All of this organization had to be closely monitored and followed up by the staff at the clinic every step of the way.

# RESULTS

The main objective of the study was to investigate whether PC-based WM training would prove beneficial for ADHD children on ADHD medication; consequently, we were interested in seeing whether there would be any differential improvement in performance on WM measures in favor of the treatment group. A second objective was to see whether any differential improvement between the groups on the various WM measures could contribute to the theoretical debate about the contents of WM.

## **PC-training gains**

All of the 23 subjects in the treatment group who started the training regime completed minimum program requirements as specified by the program developers. The gains registered by the training system at the end of the 25-day training period ranged from a minimum of 7.52% to a maximum of 46.44%; average for the group was 23.02% (7.63 SD). The ROBO-memo program developers reported that the normal training gain in earlier studies was a mean of 23%. The mean in the current study was 23.2%.



Figure 2. Distribution of training gains on PC-exercises in treatment group.

### WM outcome measures

Tables 1-9 in the Appendix provide a summary of the main outcome measures.

One-way analyses of variance (ANOVA) revealed no significant group differences at pre-test. At post-test, Visual Span forward condition ( $\underline{F}(1,43) = 4.45$ ,  $\underline{p} = .05$ ,  $\underline{Eta} = 0.10$ ; see Figure 2) and Digits Forward longest ( $\underline{F}(1,43) = 5.11$ ,  $\underline{p} = .03$ ,  $\underline{Eta} = 0.11$ ; not shown in Figure 2) were significantly higher in the experimental group. The Digits Forward total score was not, however, significantly higher in the experimental group at post-test. To check for the effect of retesting, two-tailed Paired Samples T-tests were carried out for all tests used for each group separately and described in Table 2. For the treatment group, four tests reached significant level from pre- to post-test : Visual Span Forward, (T (1,22) = -2.48, p = .02); Visual Span Backward, (<u>T</u> (1,22) = -2.79, <u>p</u> = .01); Letter-Number Sequencing (<u>T</u> (1,22) = -3.60, <u>p</u> = .00); and TMT IV, (T (1,22) = 2.48, p = .02). For the control group, two tests reached statistical significance: Digits Forward Longest, ( $\underline{T}$  (1,20) = 3.16,  $\underline{p}$  = .01); and TMT IV, ( $\underline{T}$ (1,20) = 2.90, p = .01). ANOVA between the groups showed significant differential improvement in the treatment group compared to the control group for the forward conditions of Digit Span Total and Visual Span (<u>F</u> (1,43) = 6.09, <u>p</u> = .02, <u>Eta</u> = 0.36) and (<u>F</u> (1,43) = 5.157, p = .03, Eta = 0.33), respectively. No significant differential effects were registered on reverse order tasks or other tasks (see figures 2 and 3 and tables 1-4 in Appendix).

Figure 2 provides a visual presentation of the change from pretest to posttest for treatment and control groups in the forward and backward conditions. Only results from Digit Span Total -- and not Digit Span Longest -- are presented visually in Figure 2, due to the fact that the results are highly similar in that Digit Span Longest is a subcomponent of the Digit Span Total measure. Complete results for both Digit Span Total and Digit Span Longest are presented in Table 1 and 2 of the Appendix.



Figure 2. Graphic presentation of pre- and post-test results of forward and backward condition tests.

ANOVA of pre-test and post-test results for the Letter-Number task showed no significant difference. A trend toward a differential training gain in the treatment group was detected ( $\underline{F}$  (1,43) = 2.81,  $\underline{p} = 0.1$ ,  $\underline{Eta} = 0.25$ ) (Table 3 in Appendix). ANOVA of the results on the Trail Making Task (IV) did not uncover any significant differences between groups at pre-test or post-test; nor were there any differential effects after training (Table 4 in Appendix).



Figure 3. Graphic presentation of pre- and post-test results in divided attention tasks.

The above analyses were performed on raw scores which are most relevant since the groups did not differ much in age. It could be argued, though, that use of scaled scores that account for age differences could reveal subtle differences not evident from an analysis of raw scores. The age span was approximately 3 years, and there is considerable developmental change during these preadolescent years. Scaled scores are, however, usually a rougher estimate of performance. For the sake of thoroughness, we performed the same analyses also with age corrections. Below are reported significant findings from these analyses as well as deviating findings from the raw score analyses.

WISC provides Scaled Scores for most of the tests in the WISC battery. However, when splitting total Digit Span performance into forward and backward span, no standardized scores are available. Instead, cumulative percentages relative to the norm group are provided in Appendix B of the WISC manual. Thus, the raw scores for each condition were converted to the reported cumulative percentages. The results between groups for pre- and post-tests are listed in Tables 8 and 9 in the Appendix. The percentages in Figure 5 have been inverted in order to provide a more intuitive visual presentation. Compared to the raw score analyses, results for the post-test result for longest forward were not significant, as in the analyses of raw scores. The ANOVAs of the cumulative percentages showed the same results as the analyses based on raw scores, i.e. a significant differential change between the groups from pre- to post-test for the forward condition ( $\underline{F}(1,43) = 7.73$ ,  $\underline{p} = 0.01$ ,  $\underline{Eta} = 0.39$ ), indicating a significant differential improvement in the treatment group.



*Figure 4. Graphic presentation of pre- and post-test scaled score levels in Digit Span test.* 

Scaled scores are available in Leiter for Visual Span forward & backward conditions. As in the analyses of raw scores, ANOVA of scaled scores at post-test revealed a significant differential improvement for the treatment group in the Visual Span test forward condition (<u>F</u> (1,43) = 6.32, <u>p</u> = 0.02, <u>Eta</u> = 0.13) (see Figure 5), but not in backward condition.



*Figure 5. Graphic presentation of pre- and post-test scaled score levels in Visual Span test.* 

WISC provides Scaled Scores for the Letter-number sequencing test. In contrast to the raw scores, ANOVA of the scaled scores at post-test revealed a significant differential improvement for the treatment group ( $\underline{F}(1,43) = 3.97$ ,  $\underline{p} = 0.05$ ,  $\underline{Eta} = 0.29$ ) (see Figure 6).



Figure 6. Graphic presentation of pre- and post-test scaled score levels in Letter-Number test.

Correlational analyses were conducted to examine if there were any significant correlations between gains in the training exercises and subject characteristics or outcome measures. The only correlation reaching significance was between age and PC-training gains. Investigated using Pearson product-moment correlation coefficient, there was a medium, positive correlation between the two variables ( $r^2 = 0.19$ , n = 23, p = 0.04), indicating that higher age was associated with higher training gains.

In summary, ANOVA analyses revealed a relative consistent differential change in favor of the treatment group in verbal and visual forward condition tasks, while there was no significant differential change in the verbal and visual backward condition tasks. An analysis of the scaled score values for the most part confirmed the results of the analyses of the raw score data, with the exception of the Letter-number sequencing task, in which ANOVA of the raw data did not find a significant differential change, while ANOVA of the scaled scores did find a differential change.

# DISCUSSION

The main finding is a differential improvement for the training group in forward condition verbal and visuospatial tasks compared to the control group, but not in reverse order tasks. Furthermore, the results showed neither a significant effect of training on TMT-IV, nor in the raw scores for Letter-Number sequencing task, although using scaled scores did reveal a significant differential effect between groups on this task. The prediction, based on earlier studies, was that we should expect differential improvement in the training group compared to the control group on all the tests. What happened?

#### **STM and WM Outcome Measures**

To begin with, all of the children in the intervention group completed minimum training requirements and on average posted performance gains on the PC exercises equal to children in the earlier computerized training studies showing differential improvement across both verbal and visuospatial domains (Holmes et al, 2001; Klingberg, et. al 2002 & 2005). In other words, the children in the intervention group in the current study had the same basic starting point for transferring improved program performance to other, similar task contingencies as the children in the earlier studies. The question then is why training gains in the current study only transferred to forward condition WM measures and not to reverse order tasks? One possibility is that the treatment and control groups had a small numerically different starting point on the forward condition tasks. However, even though the average is different, it does not reach a level of significance between the groups on this measure. Another explanation for the increase in the forward and not in the backward condition could be if there were a roof effect regarding the backward condition. However, as evident from the cumulative percentages, both groups performed equivalently below norm group averages both on forward and backward verbal span, leaving the same potential for improvement in both processes. The scaled scores on the Visual Span tests were nevertheless close to normal levels, but again there were no differences between forward and backward span, leaving also the same room for improvement. Thus, the starting point for the children does not seem to be a sufficient explanation for the divergence in outcome.

In the landmark, double-blind WM training study run by the Klingberg group (Klingberg et al. 2005), the authors reported significant differential improvements in verbal and visual WM for the training group. There were a total of 53 ADHD subjects in this study ranging in age from 7 to 12 years. The problem in comparing results with this study, however, is that by using a wide definition of WM "to retain information during a delay and then to make a response" (Klingberg et al, 2005, p. 177), they did not separate the results for Digit Span and Span Board into forward and reverse order subcomponents. Potentially large gains in the forward condition subtests for the treatment group could be boosting the overall differential score into significance. In the 2005 study, the authors reported effect sizes on visuospatial WM equivalent to the medication effect. The children's scores were normalized, i.e., raised 19% to within 0 to 0.3 standard deviations below the rest of the population (Klingberg et al, 2005). A significant boost in scaled scores was registered for the treatment group in the current study for forward condition verbal and visuospatial WM measures as well, but not for the reverse order verbal and visuospatial WM measures. The clear difference in forward and reverse order results in the current study seems to be a strong argument for separating the subcomponents of WM in future studies.

In the original WM training study by the same group using the same computerized training program (Klingberg et al., 2002), the authors did report separate results for forward and reverse order components of the test in the second of two experiments of the study. In the first experiment involving 14 ADHD subjects ranging from 7-15 years, they reported a significant differential improvement on the overall Span Board task for the treatment group, but there was no reporting of forward and backward subcomponents. The second experiment showed significant change from pre-test to post-test in both forward and backward conditions on the Span Board task; however, this second experiment included only 4 healthy adult males and no control group (Klingberg et al, 2002). The significant group difference in forward and backward conditions of the Span Board test was arrived at by comparing intra-individual test-retest differences between the treatment group (4 healthy males) and the placebo group (two girls and five boys ranging in age from 7-15 years) in the first experiment. The results from the current study replicate these findings only in the forward condition verbal and visuospatial tasks.

The U.K. study mentioned earlier using the same computerized training program and including 42 children ranging in age from eight to ten reported significant differential

improvements in verbal and visual WM measures and did differentiate between STM and WM in both domains (Holmes et al, 2009). An important feature of this study was that while the intervention group also trained on the adaptive version of the training program, the control group also trained, but on the non-adaptive version of the program. Thus, they did not test the effect of training per se, but rather if the new adaptive version was better than the non-adaptive version. To assess verbal and visuospatial STM and WM, the study used composite scores making it difficult to compare the results directly with the results in the current study. Digits backward was, however, one of two tests included in the study's composite verbal WM measure. The published results show that the intervention group improved significantly from pre- to post-training on all measures of Verbal STM, Visuospatial STM, Verbal WM and Visuospatial WM. However, the group training on the non-adaptive version also improved significantly on the verbal WM measure from pre-test to post-test in the study. If they should be considered a control group, then there was only a WM specific effect from the current adaptive training program on the Visuospatial WM test.

Comparing the results from subjects in the U.K. study with the subjects in the current study is somewhat problematic. The subjects in the U.K. study were not diagnosed with ADHD, but were chosen based on performing below the 15<sup>th</sup> percentile on a routine WM screening test. The reason for their low performance is not known and could be the consequence of a myriad of underlying causes, and by selecting arbitrarily low scorers one can expect a regression to the mean upon retesting. After the training, 65% of the children in the U.K. study reported that what had helped them to improve on the tests were strategies such as concentrating harder by closing their eyes or focusing more on the presented information. Perhaps these types of external strategies alone could have produced the improved results for these children and should be investigated in future studies. These types of external strategies could also have affected performance in the current study. In any event, the U.K. study did find significantly greater gains for the experimental group versus the control group for Visuospatial WM, in contrast to the results of the current study. In summary, shortcomings in the design of the previous studies make it difficult to generalize the findings, and especially to pin-point what was effective in the training. The only well controlled study -- the 2005 Klingberg et al. study -- was not designed in a way that permits separation of training effects between STM and WM.

The authors in the 2005 WM study by the Klingberg group noted that a limitation in their study was that the young subjects were not on medication and that there was a need to evaluate the effects of combining medication with training in future studies (Klingberg et al., 2005). All of the children in the current study were on ADHD medication throughout the duration of the study. So the question arises whether the effect of medication might explain the lack of differential findings for reverse order tasks compared to the earlier studies. There do not seem to be any findings in the literature indicating that ADHD medication can have a selective effect on immediate attention span at the expense of more mentally challenging tasks; quite the contrary. There must be another explanation for the discrepancy.

A detailed examination of the contents of the exercises used in the computerized training program may provide an important clue to explaining the pattern of results in the current study. None of the earlier studies investigated whether test gains could be traced back to the exact format of the computerized training exercises. Out of the 13 exercises in the training program, a total of 11 were in fact forward-oriented tasks, while only 2 involved backward-oriented mental processing skills. This means that the children in the treatment group were spending much more time training on tasks designed to increase immediate attentional span or capacity, and not the more complex mental manipulation required by more challenging, reverse order tasks. This could be a reasonable explanation of why the children in the treatment group on verbal and visuospatial forward condition tasks, and not on reverse order tasks.

Beyond the divergent operationalisations of STM and WM, the main design difference between the 2002 and 2005 studies by the Klingberg group and the current study is the use of medication by the ADHD subjects. Medication alone cannot seem to explain the difference in results. A total of 56% of the children in the treatment group in the current study posted an above-average proficiency gain on the computer-training exercises, but this learning seems to have transferred primarily to similar, simple tasks, and not to the more complex tasks. Further studies will have to be conducted to try to untangle the specific transfer effects of forward and reverse order computerized training exercises.

Correlation analyses between subject characteristics did not reveal any results to help explain the unique pattern of results in this study compared to the earlier WM training studies. The only significant correlation uncovered was that the older children seemed to benefit more from the computerized training program compared to the younger children, but this should be interpreted carefully because of the very low statistical power of the age distribution (only two nine-year olds and three 12-year-olds among the mostly 10 and 11-year-olds). Further investigations might be warranted into age-related far transfer gains from computerized training – perhaps far transfer gains are dependent on critical maturational changes emerging during these preadolescent years.

In summary, the results of the current study indicate a training effect on simple attentional capacity, but that this enhanced capacity has not generalized to more complex attentional control, i.e. no improvements in the central executive aspect of WM. The generalization or learning transfer from primarily visual tasks to better auditive capacity seems to reflect that this is not purely a training effect that is limited to tests that are similar in design to the tasks in the computerized training program. This is good news, and opens up the possibility of the training program having had an impact beyond the specific training exercises. Whether or not this is true can only be more fully discussed after more systematic data on changes in school and at home are collected at the follow-up testing seven months after post-test 1.

#### **Theoretical issue**

The intention in the current study on the theoretical level was to examine whether the systematic WM training intervention would have a dissociative effect on verbal and visuospatial STM and WM test results. Specifically, the question addressed is whether WM is best characterized by a model incorporating domain-general resources (e.g. a central executive) supplemented by domain-specific storage STM (e.g. phonological loop and visuospatial loop) in the tradition of Baddeley (2000), or by a model in which WM resources are separable across the verbal and visuospatial domains, i.e. that there is no need to differentiate between WM and STM, but only between modalities, e.g. Miyake & Shah (1996).

The authors Engle et al. (1999) investigated the issue of separability of STM and WM in a study using a wide array of neuropsychological measurements and applying confirmational factor analysis (CFA) to try to shed light on the puzzle. The alternative hypotheses were whether STM was a part of WM, whether WM was a part of STM or whether they were simply two completely different functions. The authors' findings were that STM and WM reflect two clearly distinguishable constructs, although highly related. A strong degree of

overlap between STM and WM is consistent with Baddeley and Hitch's (1974) domaingeneral model. Cowan (2008) argued further that WM is a more complex construct than STM, and argued for a construct where WM is based on activated STM memory along with central executive processes. The findings in Engle et al. (1999) were shown to be consistent with Cowan's model as well. Even though STM and WM were shown to rely on the same memory system and are thus highly correlated, WM tasks primarily engage the central executive to maintain information activated that is relevant to the current task. The differential reliance on controlled attention makes the two constructs separable both theoretically and empirically.

In the current study, the results showed clear STM performance improvements in both verbal and visuospatial domains, but not in the reverse order verbal and visuospatial WM tasks. In other words, the outcome measures registered a dissociative effect on STM and WM functions, but not fractionation of the verbal and visuospatial domains. Consistent the results reported by Engle et al. (1999), the results of the current study seem to indicate that there is a common underlying mechanism assisting the reconstruction of serial order in both verbal and visuospatial domains; this finding, again, clearly supports the domain-general view. In addition, all of the exercises in the computerized training program, which can reasonably be assumed to have been the cause of the enhanced STM performance in the treatment group, were primarily visuospatial in form. Even though the intervention group trained exclusively on visuospatially delivered STM and WM tasks, improvements were registered equally significant on verbal and visuospatial STM tasks (i.e. forward condition) posttests; and similarly, no performance improvement was registered in either verbal or visuospatial WM (i.e. reverse order) tasks posttest. This seems to be further confirmation of the results supporting the domain-general model view of WM. Nor were there any pre to post training changes registered in the TMT-IV task, which is considered a test of complex information processing due to the tax on WM by having to simultaneously process numbers and letters. The fact that the Letter-number sequencing task showed significant changes when standard scores were analyzed, means that the possibility of some effect on WM from training having taken place must not be completely dismissed. Nevertheless, out of eight WM measures (analyses of raw scores and standard scores), only one of these is significant, while all of the STM score analyses - both raw scores and standard scores - showed differential improvement.

In conclusion, the findings from the current study showing equal differential effects from training on verbal and visuospatial STM, but not on WM, seem to indicate that the theoretical structure of WM capacity is consistent with the view that there may be domain-specific components for storage, but that the critical factor for boosting capacity is a domain-general component for processing information. The results in the current study support the view that WM tasks presumably make more demands on the central executive or controlled-attention component than do the STM tasks. While most studies examining these cognitive constructs in the past have compared either clinical patient groups with normal controls or patients with impaired cognitive functioning due to disease or accident, the current investigation aimed at seeing whether manipulating aspects of the theoretical construct through a systematic learning intervention techniques based on protocols to build-up new capacities and skills through systematic, PC-based training, perhaps a new tradition of construct testing will emerge.

#### Limitations

An intervention study involving children with a diagnosed mental disorder must always strike a fine balance between clinical considerations and optimal experimental design, where the interest of the individual patient must take priority. In this study, the overall design goal was to organize a training regime and testing program as close to the clinical reality of the child involved, while upholding a strict commitment to training requirements and testing schedules in order to be comparable to other studies and potentially replicable. The overall goal was satisfied. There was nonetheless a need for intense follow-up of the children in the training program, and the members of the testing staff were keenly aware of who among the children were in the intervention group and who were receiving treatment-as-usual. While it would have been better to have the testing staff blind to the group assignment, this was not possible in the current study, and this relational variable may likely have played a role in added motivation and effort on the part of the children in the intervention group compared to the control group in terms of focus and concentration in the testing situation. Even so, any added motivational inspiration that may have infuenced the results did not push the intervention group to significant differential results in the reverse order verbal and visuospatial tasks.

Intelligence is an important factor assumed to influence learning ability and capacity. Comparing the IQ of children in this study to a study conducted in Bergen, Norway (Lundervold & Sørensen, 2008), the children in the current had almost 1 SD higher IQ figures in both verbal and perceptual domains (94 VIQ and 92 PIQ in the current study compared to 84 VIQ and 85 in the Bergen study). The ADHD children in the Bergen study, however, were chosen from a general pool of schoolchildren based on behavior symptom profiles reported by their teachers; they were subsequently formally diagnosed. Selecting only children with the most noticeable behavioral problems for an ADHD study may have distorted the sample. In another Norwegian study with ADHD children similar to the ADHD children in this study, the full IQ mean was reported to be 97 (Egeland, Johansen, & Ueland, 2009). This indicates that some populations of clinical ADHD children are not as impaired intellectually as some studies have shown, and that the subjects included in the current study are within the IQ norms for ADHD children shown in other studies.

An important lesson learned from this clinical intervention study was the role parents of the children in both the intervention group and controls played in ensuring that their children carried through to the end of the experiment. The process seemed to reinforce the child-parent relationship for both groups, and this is also a possible benefit of the training program that could be investigated in future studies.

The effect of training over the long-term is perhaps one of the most important outcomes of the study that has not been discussed in this paper. This will be the subject of later articles after the results from the follow-up, post-test 2 results have been finally collected early in 2011.

# CONCLUSION

The results of the current study with ADHD children on medication only partially replicate results found in earlier studies. Significant differential improvements in verbal and visuospatial STM were shown, but not significant differential improvements in verbal and visuospatial WM. The argument is made that the discrepancy in results compared to earlier studies may be explained by differing definitions and operationalisations of WM. Whereas earlier studies have used a wider definition of WM that mixes short-term attentional capacity with more complex mental processes, the current study differentiates operationally between the simpler STM and the more complex WM functions. The results of the current study would seem to indicate support for the division of STM and WM into forward and backward task components when measuring for potential differential gains in future training studies.

Even though the effect of the training was not as broad-reaching as earlier studies have documented, the current study did find a beneficial effect of computerized WM training for ADHD children on ADHD medication immediately after training. However, as the results of the Holmes study showed (2009), a short-term gain does not necessarily translate into a sustainable long-term gain. Nor was there evidence of any transfer of learning in the current study from improved STM verbal and visuospatial abilities to other tasks requiring divided attention. But most importantly, since the current investigation was looking into the effects of the training on WM capacity, the findings in the current study did not find differential changes in the more complex WM function, which by many has been shown to correlate closely with aptitude. Whether the selectively improved cognitive functioning found will transfer to academic gains or better functioning at home in the short and long-term was not within the scope of this paper to address. The answer to possible long-term benefits may lie in further analyses of the data collected in the ongoing overall study. Future studies will also be needed to clarify the precise content of WM that is amenable to change by computerized WM training, and the theoretical framework needed as a foundation to guide further research. The findings in the current study seem to support the well-established domain-general model.

In summing up, children diagnosed with ADHD need all the help they can get to develop into healthy, happy, prospering adults. Medication is a common treatment option, but medication alone is not enough. In the range of alternative treatment options in addition to medication, promoters of computerized WM training have touted the dramatically beneficial effects of computerized WM training. Based on the results of the current study, any overly optimistic enthusiasm should rightly be tempered, but not extinguished. The current study has shown that many ADHD children on ADHD medication will experience certain short-term attentional gains immediately after training, but they will not show the same gains on the more taxing WM tasks right after training. The long-term effect of the training and whether the short-term attentional gains will transfer to school or home environment is the subject of the ongoing project. Consequently, an opinion about whether the registered gains in the current study thus far are worth the overall investment in time and resources at the expense of other treatment options will have to wait. The verdict is not yet in, but an important next step in the investigative efforts to assess the potential of a promising, new intervention option for children diagnosed with ADHD has been taken.

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# APPENDIX

# Table 1. Results of Digit and Visual Span, forwardcondition

	Treatme	ent		Control			Differential effect:		
	(N=23)			(N=21)	ANOVA				
Digit span	Before	After	Change	Before	After	Change	F	р	Eta
forward	7.2	7.7	+0.6	7.9	7.4	-0.4	6.1	0.02*	0.13
total	(1.4)	(1.3)	(1.6)	(1.1)	(1.4)	(1.0)			
Digit span	Before	After	Change	Before	After	Change	F	р	Eta
longest	5.0	5.3	+0.3	5.2	5.1	-0.3	9.8	0.0*	0.19
forward	(0.7)	(0.8)	(0.9)	(0.7)	(0.8)	(0.5)			
Visual	Before	After	Change	Before	After	Change	F	р	Eta
span	19.9	21.8	1.9	20.5	19.8	-0.7	5.2	0.03*	0.11
forward	(3.1)	(2.8)	(3.6)	(2.5)	(3.4)	(3.9)			

# Table 2. Results of Digit and Visual Span, backward condition.

	Treatme	nt		Control			Diffe	rential e	ffect:	
	(N=23)			(N=21)		ANO	ANOVA			
	Before	After	Change	Before	After	Change	F	р	Eta	
Digit span	5.8	6.3	+0.5	5.7	6.0	+0.4	0.1	0.8	0.0	
backward total	(1.4)	(1.3)	(1.4)	(1.2)	(1.5)	(1.6)				
	Before	After	Change	Before	After	Change	F	р	Eta	
Digit span	3.3	3.5	+0.3	3.1	3.3	+0.3	0.1	0.8	0.0	
longest backward	(0.8)	(0.7)	(0.8)	(0.7)	(0.9)	(0.8)				
	Before	e After	Change	Before	After	Change	F	р	Eta	
Visual span	11.3	12.7	+1.5	11.6	12.7	+1.1	0.1	0.7	0.0	
backward	(3.1)	(2.5)	(2.5)	(2.4)	(2.7)	(3.5)				

	Treatme	ent		Control		Differential effect:			
	(N=23)			(N=21) ANOVA					
Letter-	Before	After	Change	Before	After	Change	F	р	Eta
number	12.2	14.7	+2.5	11.8	12.3	+0.5	2.8	0.1	0.06
sequencing	(3.9)	(4.4)	(3.3)	(5.5)	(5.2)	(4.6)			

## Table 3. Results of Letter-number sequencing.

\*Indicates significant difference.

## Table 4. Results of Trail Making Test, IV.

	Treatme	ent		Control			Differential effect:		
	(N=23)			(N=21)			ANOV		
	Before	After	Change	Before	After	Change	F	р	Eta
TMT, IV	144.0	115.2	+28.8	144.0	116.6	+27.4	0.008	0.9	0.01
	(56.5)	(40.5)	(55.7)	(58.4)	(46.6)	(43.4)			

	Treatment			<u>Control</u>		Differential effect:			
	(N=23)			(N=21)		ANOVA			
Letter-	Before	After	Change	Before	After	Change	F	р	Eta
number	5.39	7.35	+2.0	5.5	5.7	+0.2	4.0	0.05*	0.29
sequencing	(3.3)	(3.8)	(2.8)	(4.2)	(3.3)	(3.1)			

# Table 5. Scaled Scores for Letter-numbersequencing.

\*Indicates significant difference.

## Table 6. Scaled Scores for Visual Span, forward.

	Treatment			<u>Control</u>	Differential effect:				
	(N=23)			(N=21)	ANOVA				
Visual	Before	After	Change	Before	After Change H			р	Eta
Span	9.30	11.43	+2.13	9.76	9.14	-0.62	4.94	0.03*	0.11
forward	(3.0)	(3.6)	(3.5)	(2.95)	(3.2)	(3.9)			

	Treatme	ent		Control	Differential effect:				
	(N=23)			(N=21) ANO			VA		
Visual	Before	After	Change	Before	After	Change	F	р	Eta
Span	9.61	11.22	+1.61	9.90	11.24	+1.33	0.08	n.s.	0.00
backward	(3.3)	(2.8)	(2.7)	(2.4)	(3.0)	(3.9)			

## Table 7. Scaled Scores for Visual Span, backward.

\*Indicates significant difference.

# Table 8. Cumulative percentage of norm group onLongest span, forward, WISC-IV.

	Treatment			<u>Control</u>	Differential effect:				
	(N=23)			(N=21)	ANOVA				
Digit	Before	After	Change	Before	After	Change	F	р	Eta
Span,	83.66	76.66	+7.01	72.42	80.00	-7.58	7.73	0.01*	0.39
forward	(17.3)	(19.8)	(20.4)	(22.5)	(22.5)	(13.3)			

\*Indicates significant difference.

# Table 9. Cumulative percentage of norm group on Longest span, backward, WISC-IV.

	Treatme	ent		Control	Differential effect:				
	(N=23)			(N=21)	ANOVA				
Digit	Before	After	Change	Before	After	Change F		р	Eta
Span,	83.26	77.26	6.00	88.60	81.01	+7.59	0.06	n.s.	0.04
backward	(20.0)	(23.3)	(23.4)	(15.5)	(21.8)	(21.1)			

# Effects of working memory training on medicated ADHD preadolescents

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Computerized working memory (WM) training has been shown to improve attention and WM in ADHD. However, only unmedicated samples have been studied so far, and most preadolescents diagnosed with ADHD take medication for the condition. The aim of the present ongoing study is to investigate whether there is an additional treatment effect from computerized WM training in a typical clinical population of ADHD children on medication.

#### Method

#### Subjects and intervention

All 10-12-year-old children in Vestfold and Telemark counties (Norway) diagnosed with F90.0 Hyperkinetic disorder (ICD-10), satisfying inclusion criteria and in contact with specialized child psychiatric services were invited to participate in the study. Sixty-six children responded and all were included and randomly divided into treatment or control group. Data collected thus far on 42 of the medicated children (71% of the sample) serves as the basis for these preliminary analyses.

Subjects in the treatment group participated in a 25-day WM training program (Robo Memo) at their schools, while clinical controls received treatment-as-usual. Both groups were tested 1 week before and after intervention period. They will be retested seven months after completing the training program.

#### Measures

Short-term memory (STM) and WM memory was assessed with Visual Span (forward and reverse condition) from Leiter International Performance Scale-revised and Number recall (forward/reverse conditions) from Wechsler Intelligence Scale for Children-III edition.

The tests used to measure the impact on reading and math skills were LOGOS (Reading Fluency, Reading Comprehension, Listening Comprehension, Word Identification, Phonological Decoding, Orthographic Reading) and KeyMath (Mental computation and Problem solving).

The rating scales used to measure the effect on behavior pre and post test were Behavior Rating Inventory of Executive Function (BRIEF) (WM, BRI, MCI and GEC rated by parent and teacher).

#### **Results**

All subjects in the experimental group completed program requirements and showed significant gains in training tasks. Post-test I showed a differential improvement in the treatment group with regard to visual and auditory attention span, but no significant effects on reverse order tasks. Significant differential improvements were registered on tests measuring reading and math skills. No significant changes in behavior were reported by either parents or teachers.



#### Conclusion

The preliminary results from the study seem to indicate that ADHD children on medication can improve on measures of short-term memory and reading and math skills by training systematically on computerized working memory tasks. Confirmation of the long-term effects of the training will be needed before any conclusions or recommendations can be made.

Vestfold Mental Health Care Trust Department of Research

