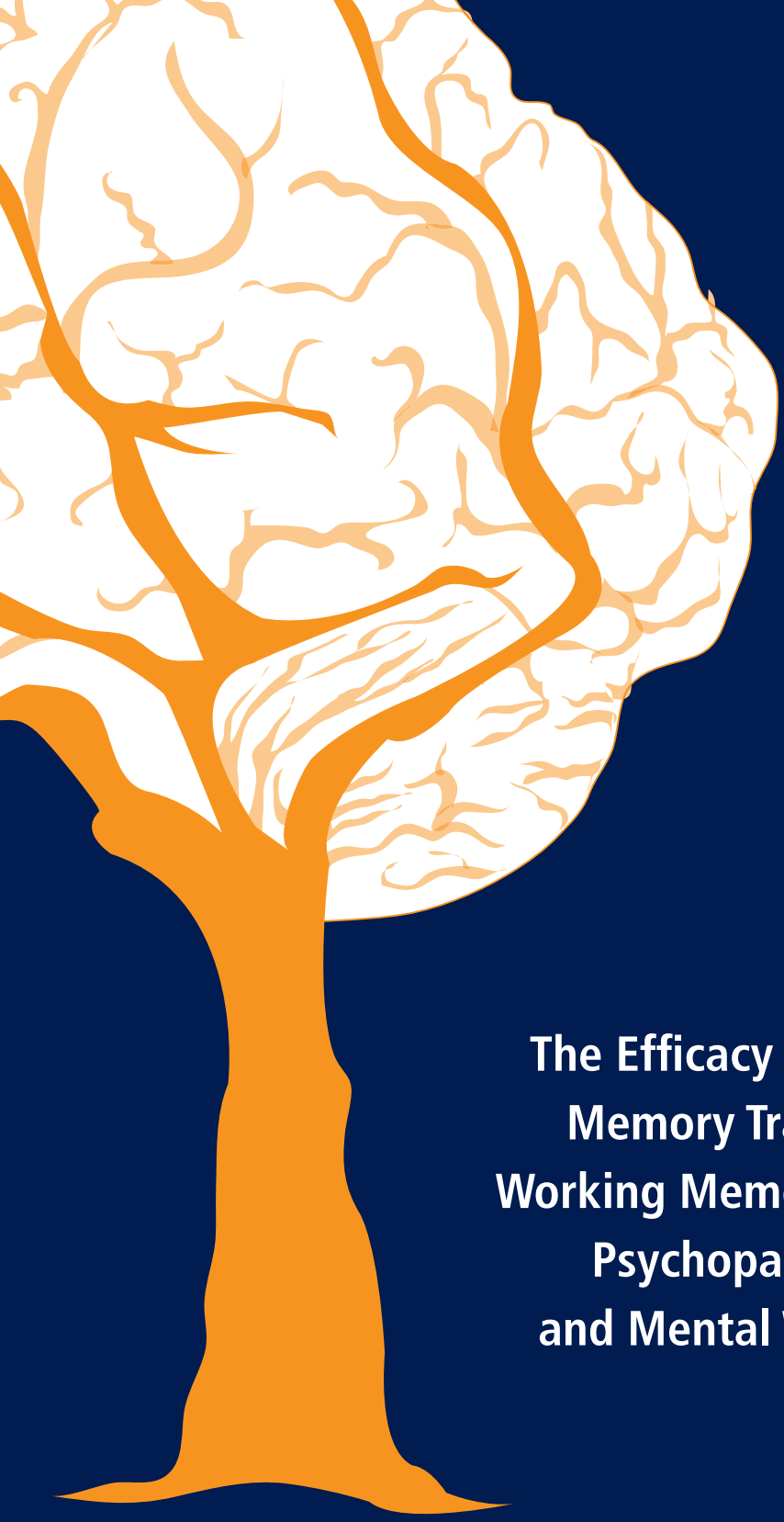

The Efficacy of Working Memory Training on Working Memory Capacity, Psychopathology, and Mental Well-being

Sabine Willemiek Wanmaker

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The Efficacy of Working Memory Training on Working Memory Capacity, Psychopathology, and Mental Well-being

De effectiviteit van werkgeheugentraining op werkgeheugencapaciteit, psychopathologie en mentaal welzijn

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Opgedragen aan Willem Wanmaker

Een ongekend voorbeeld

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Chapter 1|

General Introduction

Depression and anxiety

Mood and anxiety disorders are the most prevalent psychopathological disorders in the Netherlands (de Graaf, ten Have, Van Gool, & Van Dorsselaer, 2012). Anxiety disorders and major depression, which are the focus of this dissertation, affect respectively 10.1% and 5.2% of the Dutch population yearly. The World Health Organization (WHO) estimates that 150 million people worldwide suffer from depression (WHO, 2008) and 15% of the world population will suffer from an anxiety disorder in his/her life (Kessler et al., 2009). Approximately 85% of these patients suffer from both depression and anxiety (Gorman, 1996). This high comorbidity rate might indicate a shared underlying etiology and is reflected in similar consequences. That is, both psychiatric disorders result in significant social and personal concern, which is associated with reduced quality of life, productivity and even significantly increased mortality (Doris, Ebmeier, & Shajahan, 1999). As a matter of fact, mood and anxiety disorders are responsible for 40% of the costs for work absence and disability to work (Hutschemaekers, Donker, & Richter, 2000). Unfortunately, the prevalence of these disorders has remained stable over decades, which might imply that contemporary treatments are not able to reduce these disorders (de Graaf et al., 2012).

The most common and effective contemporary treatments for both depression and anxiety disorders are cognitive-behavioral therapy (CBT) and pharmacotherapy. CBT focuses on the modification of dysfunctional cognitions and beliefs, which cause the onset and maintenance of a depressive episode and/or clinical anxiety (Dobson & Dozois, 2001). This widely used therapy reduces symptoms significantly (Cuijpers & Dekker, 2005), but the relapse remains high (29.5%; Gloaguen, Cottraux, Cucherat, & Blackburn, 1998). Selective Serotonin Reuptake Inhibitors (SSRIs) are the most used pharmacotherapy for both anxiety (Mitte, 2005) and depression (Williams et al., 2000). This drug subdues the feelings of anxiety and depression, but does not come without side effects (Baldwin et al., 2005; Emmelkamp, Bouman, & Visser, 2008). Thus, even these most effective treatments show room for improvement in the decrease of anxiety and depression symptoms. Only 60% of the anxiety patients show reduction of their symptoms after treatment (Bruce et al., 2005; Bystritsky, 2006). In addition, 25 to 40% of the depressed patients relapse in two years, and even 87% in 15 years after initial recovery. In 13% of depressive patients this maintenance of their depressed mood results in a chronic depression (Keller & Boland, 1998). Thus, a

significant group of patients who suffer from severe feelings of anxiety and/or depression do not recover permanently (Baljon, 2007).

The cause of the persistence of these symptoms might be an underlying factor, which is not directly tackled by therapy or medication. This key factor might be a reduction in cognitive functioning, particularly working memory (WM; Eysenck, 1979, 1982; Eysenck & Calvo, 1992). The difficulties of depressed and anxious individuals (Baljon, 2007; Cuijpers, 2006) in learning (Grossman, Kaufman, Mednitsky, Scharff, & Dennis, 1994; Porter, Gallagher, Thompson, & Young, 2003; Zakzanis, Leach, & Kaplan, 1998), attention (Moritz et al., 2001; Porter et al., 2003; Zakzanis et al., 1998), concentration (Zakzanis et al., 1998), decision-making (Murphy et al., 2001) and planning (Beats, Sahakian, & Levy, 1996; Elliott et al., 1996; Moritz et al., 2001) are an expression of a deficient WM, since these are all WM functions (Baddeley, 1992).

Substance use disorder

Substance use disorder (SUD) is the physical or mental dependency of a certain drug. This severe disorder is characterized by physical dependency (like tolerance, withdrawal symptoms), mental dependency (such as craving and urges to use the substance), loss of control (using more than meant to, difficulties to stop using) and physical or social consequences of uncontrolled use (Van den Brink, 2009). In this dissertation we focus on the dependency of alcohol, cannabis, and cocaine, which are frequently used together (Wisselink, Kuijpers, & Mol, 2013). Forty-seven percent of SUD individuals searching for treatment concerns alcohol dependency. The lifetime prevalence of this disorder in the Netherlands is 2%, affecting twice as many men as women. Other risk factors are a low income, non-Western origin, and unemployment (De Graaf, Ten Have, & Van Dorselaer, 2010). That the consequences of long term alcohol abuse are serious shows its relation to 60 diseases (Kerssemakers, Van Meerten, Noorlander, & Vervaeke, 2013; Van Laar, 2009). One of the most common disturbances are cognitive deficits (Aharonovich et al., 2006; Bates, Bowden, & Barry, 2002; Pope, Hudson, Yurgelun-Todd, & Gruber, 2001), including impaired problem-solving skills, learning, short and long term memory, and perceptual-motor abilities (e.g. Allen, Goldstein, & Seaton, 1997). The fact that even five

years of abstinence cannot repair some of these deficits (Brandt, Butters, Ryan, & Bayog, 1983) indicate that cognitive consequences of alcohol abuse can be very severe.

The second largest group of SUD individuals searching for help suffer from cannabis dependency. The life time prevalence in the Netherlands of this addiction is 1.4%, of which men account for 80% (De Graaf et al., 2010). Risk factors for developing cannabis dependency are the death of a parent before the age of fifteen, low self-esteem, long term use of tobacco, antisocial behavior, and weekly use of cannabis (Coffey, Carlin, Lynskey, Li, & Patton, 2003; Von Sydow, Lieb, Pfister, Hofler, & Wittchen, 2002). Consequences of smoking cannabis are lung diseases (Kerssemakers et al., 2013; Taylor, Poulton, Moffitt, Ramankutty, & Sears, 2002) and psychopathology, like panic attacks (Van Wilgenburg, 2006) and psychotic symptoms (Fergusson, Poulton, Smith, & Boden, 2006) in individuals vulnerable for these symptoms. Severe and long-term use of cannabis is associated with small but significant deficits in recall, selective and divided attention and short-term memory (Solowij et al., 2002). Whether these cognitive consequences are only short-term effects or long-lasting is not yet known (Pope et al., 2001; Solowij et al., 2002).

Cocaine users account for 11% of individuals following treatment for SUD use (Wisselink et al., 2013). The probably underestimated (Van Laar, 2009), life time prevalence of cocaine use in the Netherlands is 5.2% (Van Rooij, Schoenmakers, & Van de Mheen, 2011). Cocaine use can result in panic attacks, paranoid psychosis, increase of blood pressure and heart failure. Consequences of chronical use are malnourishment due to loss of appetite (Volkow, 2010) and cognitive deficits, like attention, visual memory and WM (Jovanovski, Erb, & Zakzanis, 2005). However, these deficits are task and level dependent and thus vary significantly between individuals (Jovanovski et al., 2005). Common comorbid disorders of SUD in general, are major depression and anxiety disorders (Kraanen, Emmelkamp, & De Wildt, 2007). 17.1% of SUD patients suffered from a depressive episode, 32.9% from dysthymia, and 28.6% of an anxiety disorder.

Current treatments for SUD consist of psychological therapies and medication. The common first step in treatment is detoxification, to clean the body while receiving medication to reduce withdrawal symptoms (O'Brien, 2006). An often used therapy is CBT,

which focuses on the cognitive, affective, and situational triggers of substance use and provides skills to cope with these cues (Magill & Ray, 2009). CBT proved to be effective in treating SUD, but mainly on the short-term (e.g. Dodge, Krantz, Kenny, & Suciu, 2013; Magill & Ray, 2009). Community-reinforcement treatment (CRT) is one of the other often used effective treatments. The aim of CRT is to improve the patient's social network and to promote and increase motivation for behavioral change. Further, this therapy focuses on the improvement of future perspectives (Franken & Van den Brink, 2009; Roozen et al., 2004). These therapies can be combined with medication, which include agonists, antagonists, and anti-craving medicines, target addiction phenomena, like euphoria, withdrawal and craving (O'Brien, 2006). Treatment results reflect the chronicity of SUD, which needs long-term treatment (Dennis & Scott, 2007; Van Kerkhof, 2006). The fact that 80% of individuals in treatment for alcohol dependency have been treated before, confirms this notion. The characterizing impaired cognitive functioning negatively affects treatment effect in this disorder (McCrady & Smith, 1986; Franken, Rosso, & Van Honk, 2003; Goldstein & Volkow, 2002), and thus, it might explain the high relapse rate (Silverman, DeFulio, & Sigurdsson, 2012).

Working memory

Working memory is a limited-capacity system that reflects the focus of attention and the temporary activation of representations that are the contents of awareness (Jonides et al., 2008; Miyake & Shah, 1999). The system temporary stores, activates and maintains information and is therefore essential to a wide range of cognitive functions including comprehension, reasoning and learning. One of the most influential WM models is Baddeley's multi-component model of WM (e.g., Baddeley, 1992; Baddeley & Hitch, 1974; Repovŝ & Baddeley, 2006). This model consists of two components: the central executive which consists of separable executive functions and which has a wide variety of capacities and secondly, the slave systems which are responsible for short-term maintenance of information and the processing of verbal and non-verbal material (Repovŝ & Baddeley, 2006). These executive functions are involved when stored information needs to be manipulated. Furthermore, the functions are used as a source of attentional control, which not only enables one to focus attention, but also to allocate and shift attention between concurrent goals or tasks. The so-called slave systems support the central

executive to execute these functions and consist of the phonological loop, visuo-spatial sketchpad and episodic buffer. They respectively process auditory and visual information and the episodic buffer integrates all incoming information.

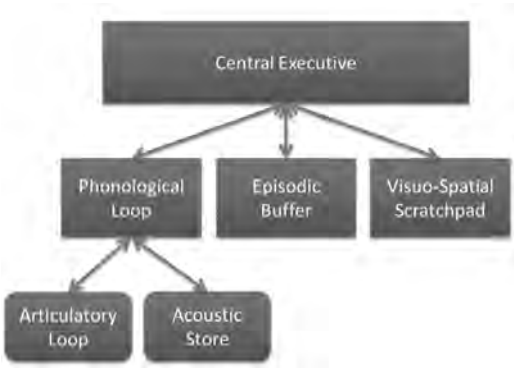

Figure 1. Working memory model of Baddeley (2000)

Depression and anxiety mostly affect the central executive of all WM components (Channon, Baker, & Robertson, 1993; Eysenck, Derakshan, Santos, & Calvo, 2007). Although neuroimaging studies confirm this finding (Bishop, 2009; Eysenck et al., 2007), recent studies argue that anxiety and depression also negatively affect the phonological loop because worry typically involves inner verbal activity (Rapee, 1993). These WM deficits express in problems and symptoms experienced by depressed and anxious individuals, such as difficulties in learning, attention, concentration (Zakzanis et al., 1998), decision-making (Murphy et al., 2001) and planning (Moritz et al., 2001; Beats et al., 1996; Elliott et al., 1996), which are all typical WM functions (Ilkowska & Engle, 2010). Although WM is involved in an array of functions, the main task of WM is to maintain its contents up to date (Friedman & Miyake, 2004; Hasher, Zacks, & May, 1999) as it has a limited capacity (Bomyea & Amir, 2011). Specifically, to prioritize goal-relevant information the contents of WM should be constantly monitored and updated, it has to inhibit negative or threatening intrusions (Miyake et al., 2000) and shift between prepotent responses and less prepotent responses (Hasher et al., 1999). Therefore, one's working memory capacity (WMC) is defined as the extent to which goal-relevant information is kept in an active state in WM, despite the interference of irrelevant information (Unsworth & Engle, 2007).

Individual differences in WMC should in theory only be relevant when goals need to be actively maintained in the face of distraction, when there is response competition, when information needs to be inhibited or suppressed and when controlled, planned memory search or error monitoring is needed (Engle, Kane, & Tuholski, 1999). The important role of WMC in distraction is reflected in a study in which individuals with a high WMC were better capable to ignore distracting information (Conway, Cowan, & Bunting, 2001) and thus showed more goal-directed behavior (Hofmann, Gschwendner, Friese, Wiers, & Schmitt, 2008). In addition, individuals with a low WMC were less able to inhibit irrelevant information when under cognitive load (Barrett, Tugade, & Engle, 2004). Furthermore, individuals with a high WMC were more capable to suppress negative as well as positive emotions compared to individuals with a low WMC. This finding could not be attributed to less *expression* of emotions in general as the groups did not differ in emotional expression. Moreover, a high WMC is associated with the capability to appraise emotional stimuli in an unemotional manner, which results in less experience and expression of emotions (Koster, Soetens, Braet, & De Raedt, 2008; Schmeichel, Volokhov, & Demaree, 2008). Neuroimaging studies confirm the essential role of WM in the processing of emotional material. Several studies found increased activation of brain areas that are associated with WM when individuals appraised emotional stimuli in an unemotional manner (Miller & Cohen, 2001; Schmeichel et al. 2008). Thus, effective functioning of WM and utilizing its capacity are not only essential to execute daily tasks (Conway, 1996), but also to process information efficiently.

Depression, anxiety and working memory

Depression may be attributable to a faulty allocation of processing resources caused by a dysfunction of the central executive component of WM. Specifically, the WM deficits of depressed individuals cause their selective processing of negative material, which maintains in their WM and lead to the continuation of a negative mood (Isen, 1984; Siemer, 2005). WM deficits in depressed patients are independent of age (Beats et al., 1996; Elliott et al., 1998; Fossati, Amar, Raoux, Ergis, Allilaire, 1999; Lockwood, Alexopoulos, Van Gorp, 2002) or the number of depression episodes (Harvey et al., 2004). WM deficits in depressed individuals are backed up by structural, functional and resting state neuroimaging research. These individuals show reduced brain activity in parietal, anterior cingulate and dorsolateral

prefrontal cortices (DLPFC) when compared with healthy controls (Bench et al., 1992; Bench, Friston, Brown, Frackowiak, & Dolan, 1993; Dolan et al., 1992; Dolan et al., 1993; Elliott et al., 1996; Okada, Okamoto, Morinobu, Yamawaki, & Yokota, 2003; Soares & Mann, 1997; Smith & Jonides, 1997; Videbech et al., 2002). The PFC and cingulate cortices have been identified as components of the neural system subserving WM and attention (Cohen et al., 1997; Courtney, Ungerleider, Keil, & Haxby, 1997; D'Esposito et al., 1995; McCarthy et al., 1996; Mesulam, 1998). Furthermore, the DLPFC is a key area in depressive mood (Pascual-Leone, Rubio, Pallardó, & Catalá, 1996). Moreover, activity in this area is correlated with rumination and this relation is mediated by WM functioning. This finding confirms the importance of the DLPFC in both depression and WM (Vanderhasselt, Brunoni, Loeys, Boggio, & De Raedt, 2013). However, it is important to note that some studies show that depressed and healthy individuals' WMC do not differ when depressed people are under distraction conditions because these conditions pre-empt some of the limited capacity of processing resources resulting in fewer resources available for rumination (Eysenck & Calvo, 1992; Foulds, 1952; Krames & MacDonald, 1985). In sum, increasing the ability to manage the WM contents might help individuals to control negative or ruminative thinking.

Numerous models attempt to explain depression and anxiety in a neurocognitive way. To give thorough background information regarding the link between these disorders and executive functioning, I focus on three models. The model of De Raedt and Koster (2010) (Figure 2) proposes that executive control is the crucial link between cognitive and biological vulnerability of depression after recurrent episodes. That is, decreased inhibitory control and maintained attention for negative information lead to an impaired ability to stop negative elaborative processes such as rumination, which result in sustained negative affect and recurrent depressive episodes. Specifically, according to the model a stressor in the environment of a depressed individual is the onset of the process resulting in a depressive episode. The stressor activates negative cognitive schemas and dysregulates the hypothalamic-pituitary-adrenal axis (HPA). This dysregulation is caused by hypercortisolism during depressive episodes and results in increased reactivity to stressors and dysregulation of serotonin. The serotonin dysregulation leads to decreased activity of the DLPFC brain areas, which are important for attentional control. Reduced activity in the

DLPFC is linked with prolonged activation of the amygdala in response to stressors in the environment. Increased amygdala activity through reduced frontal control leads to sustained negative affect. The reduced prefrontal control in interaction with depressogenic schemas leads to the impaired ability to exert attentional inhibitory control over negative elaborative processes such as rumination.

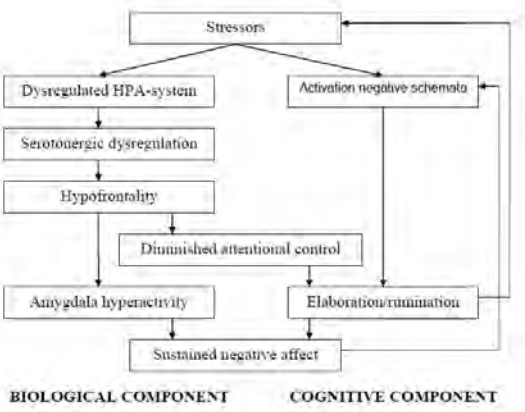

Figure 2. Model of De Raedt & Koster (2010)

Another model considers a *Default Mode Network* (DMN) dysregulation as a neural substrate of depression. The DMN is a group of brain regions, located mostly medially, which show heightened and coherent activity during rest and reduced activity during cognitive tasks (Raichle et al., 2001). In contrast, depressed individuals do not show this reduction of activity during cognitive tasks (Sheline et al., 2009). Their sustained activity is thought to be the reflection of enhanced ruminative processes during their depression. The exact relation between DMN dysregulation and depression is still unclear. Some evidence indicates that DMN abnormalities are directly responsible for causing most depressive-like symptoms, like rumination. Other findings suggest that WM dysfunctions, problem solving difficulties and information integration problems cause these DMN abnormalities (Jack et al. 2013; Zhou et al., 2010). In other words, while the existence of DMN abnormalities in depression is clear there is no consistency whether DMN abnormalities directly or indirectly cause depression symptoms.

A cognitive system imbalance might also be the cause of anxiety. High-anxious individuals show especially WM deficits when under cognitive load or in stressful situations (Calvo & Ramos, 1989; Darke, 1988; Eysenck & Derakshan, 1998; MacLeod & Donnellan, 1993; Sorg & Whitney, 1992). These deficits may be explained as the consequence of an imbalance in the interplay between two attentional systems. Firstly, an amygdala-centered threat detection system that is hyperresponsive in anxious individuals. Secondly, a prefrontal attentional control system that is critical for the inhibition of irrelevant and distracting information and that is assumed to be weakened in anxious individuals (Bishop, 2009; Eysenck et al., 2007; Mathews & Mackintosh, 1998). This imbalance is reflected in their WM deficits like shifting between task demands, inhibition of attention and updating new information (Eysenk et al., 2007). Furthermore, they have difficulties with the entry and processing of new information (Sorg & Whitney, 1992) and are quickly distracted by irrelevant information (Christopher & MacDonald, 2005). This distracting information might consist of external threatening information or internal rumination and result in less attention to execute the task and thus, reduced performance (Eysenck et al., 2007). However, because anxious individuals are more motivated to perform well than non-anxious individuals, they compensate for the interference from these task-irrelevant thoughts by expending more effort in the task (Locke, 1968). Therefore they use most, if not all, attentional resources that are not being allocated elsewhere (Eysenck & Calvo, 1992). Basten, Stelzel and Fiebach (2011) used functional Magnetic Resonance Imaging (fMRI) studies to explore whether this compensation was reflected in the DLPFC, which is responsible for executive control in attention and plays an important role in inhibiting irrelevant information (Botvinick, Cohen, & Carter, 2004). Indeed, they found an increased DLPFC activation in high-anxious individuals, which they interpreted as an attempt to compensate for the suboptimal connectivity within the cortical network subserving task performance. They concluded that a general (i.e. not thread-specific) impairment of attentional control leads to reduced neural processing efficiency in anxious individuals. In sum, executive functioning seems to be diminished in anxiety as well as depression.

Substance use disorder and working memory

Individuals with a diagnosis of SUD often suffer from cognitive deficits (e.g. Aharonovich et al., 2006; Bates et al., 2002; Pope et al., 2001). WM is one the cognitive

systems impaired by these deficits (Ambrose, Bowden, & Whelan, 2001; Bolla, Brown, Eldreth, Tate, & Cadet, 2002; Jovanovski et al., 2005). One's WMC is critical for controlling behavior (Goldstein & Volkow 2002), like attentional control (Kane, Conway, Hambrick, & Engle, 2007; Unsworth & Spillers, 2010) and response inhibition (Bobova, Finn, Rickert, & Lucas, 2009; Kane et al., 2007), which are all decreased in SUD individuals (Lundqvist, 2005; Ratti, Bo, Giardini, & Soragna, 2002). Therefore WM impairments have been associated with addiction-related behavior, such as impaired decision making (Noël, Bechara, Dan, Hanak, & Verbanck, 2007), a high rate of delay discounting (Bobova et al., 2009; Shamosh et al., 2008), self-reported impulsivity (see for a review: De Wit, 2009), and an attentional bias for substance related cues (Field & Cox 2008; Franken, 2003). These cognitive impairments contribute in two ways to substance abuse and dependency. Firstly, cognitive deficits, like impaired control, can increase drugs seeking behavior. Secondly, cognitive impairment leads to less participation in treatment programs, as a certain level of cognitive abilities is needed to comply with the therapy modules (Aharonovich et al., 2006; Bates et al., 2002; Crean, Crane, & Mason, 2011).

One of the cognitive impairments that plays a significant role in the onset and maintenance of SUD is the high level of impulsivity of these individuals (De Wit, 2009; Gunn & Finn, 2013; Perry & Carroll, 2008). They have a predisposition for fast, unplanned reactions to stimuli, without taking into account any negative consequences (Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001). Another expression of their impulsivity and their decreased WMC is their impaired decision making (Bechara & Martin, 2004), showed by delay discounting. Several studies show one's WMC is linked to delay discounting (Bobova et al., 2009). For instance, a loaded WM results in more delay discounting (Dretsch & Tipples, 2008; Hinson & Whitney, 2006; Hinson, Jameson, & Whitney, 2003). Another link between WM and substance dependency is attentional control. SUD individuals are characterized by decreased attentional control due to a lower WMC (Hester & Garavan, 2005), which results in their attentional bias for substance related cues (Franken & Van den Brink, 2009). Furthermore, their bias for substance related cues plays a large role in the maintenance of this disorder as it induces craving (Franken & Van den Brink, 2009). In sum, WM deficits in SUD individuals influence the onset and maintenance of their behavior and thus, may be important factors to focus on in treatment of this psychopathology.

Deficits in working memory key processes

WM is not a unitary construct but involves several separable key processes such as to update information, to inhibit irrelevant processes or responses and to shift attention between stimuli or manage multiple tasks (Jonides et al., 2008; Miyake & Shah, 1999; Nee & Jonides, 2008). The key process 'updating' includes three subprocesses; firstly, monitoring and coding incoming information for relevance to the task, secondly, maintaining task relevant information in WM and thirdly, replacing old, no longer relevant information with newer, more relevant information (Morris & Jones, 1990). The goal of these processes is to deactivate irrelevant information in long term memory (Anderson & Spellman, 1995; Rosen & Engle, 1998). Depressed patients and healthy controls do not differ in this first subprocess. That is, both groups can stop entry of irrelevant material into WM equally effective. However, they differ on the third updating subprocess since depression leads to an impaired ability to remove negative information from WM once it has entered (Whitmer & Banich, 2007; Joormann & Gotlib, 2008; Levens & Gotlib, 2010). These updating deficits are restricted to negative information as depressed individuals have no difficulties in updating positive material (Joormann & Gotlib, 2008). The updating difficulties found in depressed individuals, which lead to maintenance of negative material in WM, are thought to be one of the causes of rumination (Joormann & Gotlib, 2008) As rumination is one of the vulnerabilities of relapse (Michalak, Hölz, Teismann, 2011) therapies that attempt to improve this essential deficit would be promising. In contrast to these findings in depressed individuals, anxious individuals do not show diminished updating capabilities.

Shifting, the second WM key process refers to the skill to shift attention between different tasks, mental sets or operations (Miyake, Friedman, Emerson, Witzki, Howerter, & Wager, 2000). A wealth of data suggests that an individual's ability to apply attentional control to emotional mental representations is critical to effective emotion regulation (e.g. Gross & Thompson, 2007). Indeed, depressive patients show difficulties in shifting between negative and positive information (Harvey et al., 2004; Rogers et al., 2004), as they focus on negative information (Murphy et al., 1999). The shifting dysfunction persists even in individuals that recovered from depression (Paelecke-Habermann, Pohl, & Leplow, 2005). This finding emphasizes again that WM dysfunctions might be an underlying factor for

relapse in depression. Furthermore, high-trait anxious individuals show the same shift inability but their difficulties are particularly related to the shift away from threatening information (MacLeod & Mathews, 1988). Thus, depressive as well as anxious individuals show emotional shifting deficits, which might be a cause for their diminished emotion regulation.

The third WM key process, inhibition, ensures that irrelevant information does not enter consciousness. This process consists of two subprocesses (Friedman & Miyake, 2004; Hasher et al., 1999). One type of inhibition involves controlling automatically triggered prepotent responses in order to carry out an effortful response. The other subprocess refers to the ability to resist interference from information that was previously relevant to the task but has since become irrelevant because of change in context (Friedman & Miyake, 2004; Hasher, 1999). In anxious and depressed individuals this breakdown of inhibitory processes underlies the enhanced elaboration of negative information, which results in rumination (Hester & Garavan, 2005; Linville, 1996; Ursin, 2005). In daily life these inhibition deficits lead to their difficulty in suppressing intrusive thoughts, which result in more negative or threatening thoughts about aversive events in the past (Verwoerd, Wessel, & de Jong, 2009; Harvey et al., 2004).

Neurobehavioral evidence confirms these inhibition difficulties in anxious patients. Individuals suffering from PTSD showed reduced brain activity during inhibition tasks, compared with healthy controls. In other words, they have difficulties suppressing or inhibiting their thoughts about their experienced trauma (Falconer et al., 2008). The inhibition problems of depressed as well as anxious individuals are persistent, even after reduction of their symptoms (Joormann, 2004; Joormann en Gotlib, 2007; Paelecke-Habermann et al., 2005). In sum, depression and anxiety disorders are associated with diminished WM processes, which express in their daily symptoms, like rumination. Moreover, the reduced capability to manage the incoming and entered information is persistent, which confirms the idea that these deficits might be a keyfactor in relapse of anxiety and depression.

Rumination

One of the most important consequences of a deficit in the WM key process inhibition is ruminative thinking; repeated uncontrollable negative thoughts that interfere with the ability to concentrate and carry out daily activities (Nolen-Hoeksema, 2000; Birrer, Michael, & Musch, 2007; Reynolds & Brewin, 1999). Both depressed and anxious individuals suffer from this thinking style, but the content differs slightly. Depressed individuals mainly focus on their symptoms and situation, while anxious individuals mainly focus on possible future negative events (Eysenck et al., 2007). Rumination involves difficulties in controlling the contents of WM, like negative thoughts (Hertel, 1997; Linville, 1996; Joormann, 2005). A study of Borkovec, Robinson, Pruzinsky and DePree (1983) and colleagues confirms this result, as it showed that high ruminators – in contrast to low worriers – reported uncontrollability of negative thought intrusions once ruminating is initiated.

These intrusions are activated in the long term memory and capture WM (Geraerts, Merckelbach, Jelicic, & Habets, 2007; Wessel, Overwijk, Verwoerd, & de Vrieze, 2008; Williams et al., 2007). Thus, rumination consumes WM resources, resulting in a reduced capacity to perform the target cognitive task (Eysenck & Calvo, 1992). This reasoning is illustrated by studies where high ruminators compared to low ruminators had less residual WMC when worrying than when thinking about a nonworry topic (Rapee, 1993; Hayes, Hirsch, & Mathews, 2008). Thus, high ruminators have fewer attentional resources available to redirect their thoughts away from intrusions (Hayes et al., 2008) and from irrelevant negative information (Hertel, 1997; Joormann, 2005; Linville, 1996), resulting in sustained negative affect. These findings explain their difficulty to recover from a negative thought pattern and thus, from their depression and/or anxiety (Nolen-Hoeksema, 2000).

To explore the key role of WM and thus, the role of WMC, in inhibition of ruminative thoughts studies compared individuals with high and low WMC. As hypothesized, a lower WMC was associated with higher levels of intrusive and avoidant thinking (Klein & Boals, 2001), while a higher WMC was linked with experiencing fewer intrusions (Brewin & Smart, 2005; Rosen & Engle, 1998). Results of a study by Watkins and Brown (2002) suggest that rumination directly influences WMC. That is, depressed patients which were exposed to a rumination induction showed worse executive functioning compared to healthy controls,

but the groups were equal in WMC when the depressed group was not ruminating. This result is controversial as the majority of studies show that WM deficits in depressed and anxious individuals are persistent (Paelecke-Habermann et al., 2005; Joormann, 2004; Joormann & Gotlib, 2007). For example, Zetsche & Joormann (2011) and De Lissnyder et al. (2012) argue one's WMC can predict rumination and depressive symptoms after 6 months. Furthermore, efficient cognitive control seems to be important in the inhibition of intrusions after exposure to a traumatic event (cf. Anderson, 2003; Anderson & Green, 2001). The causal direction of the relationship between rumination and the difficulty in ignoring irrelevant negative information was studied using a training in inhibition of irrelevant negative information. Trained individuals showed a trend toward improved inhibition and a reduction in rumination, but not in depressive symptoms. This finding suggests that decreased inhibition abilities cause rumination (Daches, Mor, Winquist, & Gilboa-Schechtman, 2010).

Inconsistencies in working memory research

Despite the commonly accepted cognitive dysfunctions in anxious, depressed and SUD inviduals, it is important to note that not all attempts to characterize cognitive functions in these individuals have been conclusive. A number of studies argue that anxiety and depression are not significantly associated with one's cognitive functioning (Barch, Sheline, Csernansky, & Snyder, 2003; Grant, Thase, & Sweeney, 2001; Sweeney, Kmiec, & Kupfer, 2000). For example, in a study of Channon and colleagues (1993) depressed patients performed equally as healthy individuals on short-term memory tasks. This result is in line with Harvey et al. (2004), who did not find any differences between those groups on WM tasks. Furthermore, Egeland et al. (2003) state that only speed processing and selective attention are impaired in depressed individuals, but not executive functioning. Other studies argue that cognitive deficits are indeed minimal in young patients with mild depressive symptoms (Barch et al., 2003; Grant, et al., 2001), but are present in elderly depressed people and severely depressed inpatients with psychotic features (Grant et al., 2001). These literature inconsistencies may be caused by variations in characteristics of the studied patient samples, like their depression severity, which is especially important in neuropsychological functioning in depression (e.g. Cohen, Weingartner, Smallberg, Pickar, & Murphy, 1982; Elderkin-Thompson et al., 2003; Ravnkilde et al., 2002). Other factors that

may cause inconsistencies are variation in motivation (e.g. Schmand et al., 1994; Beats et al., 1996; Channon et al., 1993), age (e.g. Burt, Zembar, & Neiderehe, 1995; Sobin & Sackeim, 1997) and medication status (e.g. Sobin & Sackeim, 1997). Furthermore, task characteristics, like feedback (e.g. Elliott, Sahakian, Herrod, Robbins & Paykel, 1997), the emotional valence of stimuli (e.g. Denny & Hunt, 1992; Watkins, Mathews, Williams, & Fuller, 1992) and the level of the tasks could also contribute to these inconsistencies in findings. For instance, the difference in WM between healthy and depressed individuals seems to be more pronounced when using relatively easy tasks (Hertel, 1998, 2004; Joormann, Nee, Berman, Jonides, & Gotlib, 2010). Easy tasks, that do not require participants to fully engage with the task and do not control participants' attention, permit rumination and mind wandering and therefore, are sensitive to individual differences in cognitive control and in the use of effective strategies. Although the majority of studies conclude anxious and depressed individuals show significant WM deficits (e.g. Basten et al., 2011; Bishop, 2009; Harvey et al., 2004, Joormann & Gotlib, 2008; Whitmer & Banich, 2007) future research has to focus on task and participant characteristics that are determinative in their expression.

Studies comparing WMC of SUD individuals and healthy controls show inconsistent results as well (e.g. Jovanovski et al., 2005). Although most research concludes that SUDs have lower performance levels on WM tasks (e.g. Ambrose et al., 2001; Bolla et al., 2002; Jovanovski et al., 2005), this is not confirmed by all studies (Crane, Schuster, Fusar-Poli, & Gonzalez, 2013; Kanayama, Rogowska, Pope, Gruber, & Yurgelun-Todd, 2004; Schweinsburg et al., 2008; Smith, Longo, Fried, Hogan, & Cameron, 2010). However, brain activation of both groups differs, which might suggest that they use different brain regions or pathways to perform similarly (Batalla et al., 2013; Crane et al., 2013; Jovanovski et al., 2005; Kanayama et al., 2004; Padula, Schweinsburg, & Tapert, 2007; Schweinsburg et al., 2008; Smith et al., 2010) and which may explain the inconsistent results.

Training the working memory

The majority of evidence indicates that WM deficits are persistent, as they are still present in abstinent SUD individuals (Schweinsburg et al., 2008; Verdejo-García, Bechara, Recknor, Pérez-García, 2005) and individuals who have recovered from depression

(Goeleven, DeRaedt, Baert, & Koster, 2006; Joormann, 2004; Joormann en Gotlib, 2007; Hasselbalch, Knorr, & Kessing, 2011) or anxiety (De Lissnyder, Koster, & De Raedt, 2012). The maintenance of rumination reflects their sustaining inability to control the content of their WM. These maintaining deficient WM processes might be a vulnerability factor for depression and anxiety (De Lissnyder et al., 2012; Onraedt, Koster, Geraerts, De Lissnyder, & De Raedt, 2011). As medication has no effect on cognitive performance (Amado-Boccara, Gougoulis, Poirier Littré, Galinowski, & Lôo, 1995) another treatment for this underlying factor must be thought of. A WM training may be a suitable candidate as it showed good effects in a range of neurological diseases and diverse psychopathology, such as ADHD, schizophrenia, alcohol abuse, stroke and Multiple Sclerose (MS; Åkerlund, Esbjörnsson, Sunnerhagen, & Björkdahl, 2013; Houben, Wiers, & Jansen, 2011; Klingberg et al., 2005; Subramaniam et al., 2012; Vogt et al., 2009; Westerberg et al., 2007). A WM training consists of several WM tasks that are trained by the participants. The effect of a WM training can be measured on three levels; the direct training effect which is the effect of practicing the training tasks, secondly, near transfer, measured by tasks with the same cognitive aspect and lastly, far transfer, which is the generalized effect on WM related constructs and usually the intended effect. For example; a WM training for depressed patients might result in a training effect, near transfer to other – nontrained– WM tasks and far transfer to depression symptoms.

Since people advance through test levels a direct training effect is typically found. Of more importance is near and far training transfer. Several studies found indeed evidence for near transfer after a WM training. Like a study in which healthy young and old adults executed three updating tasks for 11 hours training in total. They improved significantly in a nontrained updating task compared to a passive control group (Dahlin, Nyberg, Bäckman, & Neely, 2008; Li et al., 2008). Although this effect was robust as it remained significant at an 18-month follow-up measurement, no significant differences were found on three WM tasks which did not measure updating. This result is in line with the argument of critics that a training effect will only transfer to other functions and tasks with the same underlying neural networks (Olesen, Westerberg, & Klingberg, 2004; Dahlin, Neely, Larsson, Bäckman, & Nyberg, 2008; Dahlin et al., 2008).

Conversely, an updating WM training of Jaeggi, Buschkuehl, Jonides and Perrig (2008) resulted in far transfer since participant's fluid intelligence improved. This result is in line with studies in which a WM training resulted in far transfer in individuals whose low WMC is a limiting factor for academic performance or in daily life (Klingberg et al., 2005). An example of this are studies which showed that training the WM of children with a poor WM result in better memory for instructions (Klingberg et al., 2005, Holmes, Gathercole, & Dunning, 2009), improvement of reading abilities (Dahlin, 2011; Loosli, Bushkuehl, Perrig, & Jaeggi, 2012) and academic abilities (Holmes et al., 2009; Thorell, Lindqvist, Nutley, Bohlin, & Klingberg, 2009). Furthermore, a WM training in adolescents with intellectual disabilities resulted in an increase of their STM, their math abilities and memory for stories (Van der Molen, Van Luit, Van der Molen, Klugkist, & Jongmans, 2010; Perrig, Hollenstein, & Oelhafen, 2009). Elderly people also profited from WM training show their improvement on STM, fluid intelligence, processing speed and inhibition (Borella, Carretti, Riboldi, & De Beni, 2010). Most of these effects remained significant at 3-month (e.g. Klingberg et al, 2005; Van der Molen et al., 2010) and 6-month (e.g. Borella et al., 2010, Holmes et al., 2009) follow-up measurements. Not only intellectual disabilities but also symptoms of physiological disorders reduce as a result of WM training. For instance, the cognitive deficits that individuals who recover from a stroke usually experience were reduced (Westerberg et al., 2007). Furthermore, multiple sclerose (MS) patients were less tired and their mental speed was improved after training their WM (Vogt et al., 2009).

These promising results lead to exploration of WM training for individuals suffering from psychopathology, as interference from irrelevant representations are proposed to reduce their WMC (Bjorklund & Harnishfeger, 1990; Enright & Beech, 1990; Frith, 1979). Klingberg did the pioneer work by training children with ADHD. WM training indeed improved individuals' cognitive functions like attention, response inhibition and reasoning abilities (Chein & Morrison, 2010; Klingberg, Forssberg, & Westerberg, 2002; Klingberg et al., 2005). Moreover, the trained children suffered from less ADHD symptoms, such as hyperactivity, impulsivity and motor activity, that is, less head movements. Not only children but also adults profited from a WM training, reflected in their improved executive functioning. These training effects maintained for at least three months (Klingberg et al., 2005). In addition, a study of Houben and colleagues (2011), which trained individuals with

problematic drinking behavior, confirms the positive effect of an improved WM on the control of behavior. A weakened WM causes automatic impulses that dominate this behavior. Training the WM, and thus the control over these impulses, resulted in reduced alcohol consumption for more than 1 month after the training. Moreover, the indirect effect of training on alcohol use through improved WM was moderated by participant's levels of automatic impulses. In other words, increasing WM resulted in reduced alcohol consumption in participants with relatively strong automatic preferences for alcohol. Another study in SUD individuals aimed to tackle delay discounting with WM training (Bickel, Yi, Landes, Hill, & Baxter, 2011). The training indeed resulted in an increase of preference for delayed, but larger rewards. Results of these studies suggest that training WM may be an effective strategy to reduce substance use by improving related behavior, like control over automatic impulses and reducing delay discounting. Even symptoms of very severe psychiatric disorders like schizophrenia reduce after training WM. Training schizophrenic patients' aberrant WM processes (Lee & Park, 2005) resulted in improvement of social functioning, a decrease of behavioral problems and an improvement of quality of life (Subramaniam et al., 2012). Neuroimaging findings in schizophrenic patients, who trained their WM, confirm increased activity in the prefrontal brain area (Wexler, Anderson, Fulbright, & Gore, 2000), which is involved in WM. In sum, WM training does not only result in improved functioning in people suffering from a low WMC but show positive effects in a variety of both psychopathological and physic disorders as well.

Although depression and anxiety are also characterized by WM deficits, to our knowledge no attempt to decrease their symptoms with a WM training has been executed in patients suffering from these psychopathology. The potential effect of such training is supported by several other studies that adapted the cognitions of this particular group. For example, depressed individuals could learn to use explicit strategies to inhibit or forget negative memories (Hertel, 2004). In addition, the modification of maladaptive interpretations reduced depressive intrusions (Holmes, Lang, & Shah, 2009). Furthermore, Siegle, Ghinassi, and Thase (2007) showed that cognitive control training was a significant addition to treatment as usual (TAU) -medication, group sessions and environment therapy- in treating depression and rumination. WM training with an emotional content even resulted in gains of emotion regulation in healthy students (Schweizer, Grahn,

Hampshire, Mobb, & Dalgleish, 2013). This effect was associated with greater activity in brain regions related to affective control, notably the subgenual anterior cingulated cortex. However, not all studies show merely promising results. Owens, Koster, and Derakshan (2013) showed a gain in WMC in dysphoric participants, measured with behavioral and neural assessments, but no effect of training WM on depression. In addition, a recent study of Onraedt and Koster (2014) showed no effect of training on WMC and no effect on rumination in high ruminators. Nevertheless, as there is a strong link between WM deficits and psychopathology, WM training seems to improve behavior and cognition in various population, and new treatment is essential to reduce relapse in these populations, we think it is still valuable to explore the effect of WM training in depressed and anxious individuals. Before this question is elaborated we focus on the neuronal changes as a result of WM training.

Neuronal changes as a result of WM training

Neuronal changes from the intracellular level to functional organization of the cortex reflect the improvement of WM (Buanomano & Merzenich, 1998; Klingberg, 2010). Before we discuss evidence more extensively, it is important to note that aspects of brain activity associated with superior capacity are still matters of debate. Nevertheless, the most consistent evidence from neuroimaging studies in humans has mapped WM-related activity to both sensory association cortices and PFC (Linden, 2007; Curtis & D'Esposito, 2003). A part of these areas show specificity to the sensory modality of the stimuli while other areas are activated more generally, like the intra-parietal cortex and the DLPFC (Linden, 2007; Curtis & D'Esposito, 2003; Klingberg, Kawashima, & Roland, 1996). These areas are activated across several modalities as well as in tasks that require control of attention. These findings are confirmed by correlations between WMC and individual differences in activity (Gray, Chabris & Braver, 2003; Lee et al., 2006; McNab & Klingberg, 2008; Todd & Marois, 2004; Vogel & Machizawa, 2004) and when comparing children and adults (Crone, Wendelken, Donohue, Van Leijenhorst, & Bunge, 2006; Kwon, Reiss, & Menon, 2002; Olesen, Macoveanu, Tegnér, & Klingberg, 2007; Scherf, Sweeney, & Luna, 2006).

Moreover, neural systems that underlie WM show direct plasticity of training WM (Olesen, Nagy, Westerberg, & Klingberg, 2003). A 5-week WM training lead to increased prefrontal and parietal cortex activity and this change in brain activity was correlated with performance outside the scanner. Hempel et al. (2004) even found training-related brain activation after 2 weeks of training. However, this activity decreased after 4 weeks of training while performance consolidated. Another factor that cause decrease of brain activity is the change of strategy during training and repeated presentation of stimuli (Schacter, Wig, & Stevens, 2007). These changes in activation support the hypothesis that training WM is mediated by different neuronal mechanisms, depending on factors like training history and training content. Training WM, therefore, may lead to a change in predominance of one of these mechanisms triggered by the ongoing requests on manipulation, storage, and attention during training.

Another recent line of research focuses on the role for dopamine in WM training, specifically the effect of WM training on the density of dopamine D1 and D2 receptors (McNab et al., 2009). The dopamine system is of particular interest in WM training because dopamine is important for both WM performance (Luciana, Depue, Arbisi, & Leon, 1992; Müller, von Cramon, & Pollmann, 1998) and neural plasticity (Stroemer, Kent, & Hulsebosch, 1998), which is essential for WM training effect. McNab et al. (2009) report an inverted-U function relation between training-related performance and D1 receptor density. This result is in line with animal studies showing that small amounts of D1-blocking agents can enhance WM-related activity, whereas large doses impair WM (Vijayraghavan, Wang, Birnbaum, Williams, & Arnsten, 2007; Williams & Goldman-Rakic, 1995). A study of Bäckman et al. (2011) which found increased dopamine activity during and after training WM confirms the pivotal role of dopamine receptor activity in WM. These findings are consistent with studies showing WM deficits in patients suffering from brain disorders involving dopamine pathology, such as schizophrenia and Parkinson's disease (Gold, Goldberg & Weinberger, 1992; Robbins et al. 1994). Thus, preliminary evidence seems to propose a causal role of dopamine in WM training performance.

In sum, although a large amount of studies find interesting associations between WM and brain areas there is currently no clear pattern of results that point to a specific

neural mechanism that would underlie training and/or transfer effects. The results are inconsistent; some studies report increase of activation, while others find diminished activation or a mixture of both trends. This inconsistent pattern might be due to certain factors that may moderate some of the neural effects, like training length (e.g. Basak, Boot, Voss, & Kramer, 2008; Hempel et al., 2004; Jaeggi, Buschkuehl, Jonides, & Perrig, 2008), task difficulty or task demands (Jolles, Grol, Van Buchem, Rombouts, & Crone, 2010), individual differences in pre-existing WM ability and/or in training performance (Bellander et al., 2011; Jaeggi, Buschkuehl, Jonides, & Shah, 2011), gender (Neubauer, Bergner, & Schatz, 2010), age (Dahlin et al., 2008; Karbach & Kray, 2009; Schmiedek, Lövdén, & Lindenberger, 2010), or even motivational processes such as the participants' effort directed to the task (Jaeggi et al., 2011; Neubauer & Fink, 2009). Thus, the identification of neural correlates of training-induced improvements has many caveats, since there occur not only many parallel behavioral changes during the course of training but there is also an array of methodological issues.

Critical notes on working memory training

Although the results of WM training are in general promising and commercial applications are already launched (e.g., CogMed (www.cogmed.com), Cognifit (www.cognifit.com) and Jungle Memory (www.junglememory.com)), both the clinical relevance and the utility of the cognitive training programs is not fully clear. A recent meta-analysis of Melby-Lervåg and Hulme (2013) concludes that memory training programs seem to result in short-term, specific training effects only and not in generalized effects, as some of these programs pretend to achieve. The meta-analysis consists of 23 studies with randomized-control trial or quasi-experimental without randomization designs, which investigated a treatment and included a treated or untreated control group. It is important to note that they did not include studies concerning training severe psychopathology, such as addiction and schizophrenia (Houben et al., 2011; Subramaniam et al., 2012).

The authors have several explanations for the contradiction of the positive results of the individual studies and the result of their meta-analysis. Firstly, some of the analyzed studies only use untreated control groups. They state that studies with such designs typically overestimate the transfer effects. This statement is confirmed by the failure to

replicate findings of studies with such design (Bergman Nutley et al., 2011; Jaeggi et al., 2011). Secondly, some of the analyzed studies used multiple significance tests without correcting for that, which might have led to a large Type I error rate (Shadish, Cook, & Campbell, 2002; Melby-Lervåg & Hulme, 2013). Another methodological issue is the lack of near-transfer effects on all measures while finding far-transfer effects (e.g. Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Jaeggi et al., 2010). This pattern of results is difficult to interpret; the authors even suggest artifacts or statistical effects cause them, like regression to the mean. Thus, Melby-Lervåg & Hulme are skeptical about the promises made by commercial trainings and the conclusions of some studies. Their skepticism also concerns the theoretical foundation of the training programs, which is the so-called "physical-energetic" model. This model states that an increased capacity is reached by repeatedly "loading" a limited cognitive resource like WM, like a muscle that grows by repeated exercise. Conway and Getz (2010) also temper the enthusiasm about the effects of WM training, especially on intelligence. They argue that fluid intelligence, general cognitive ability, and WM, are still such complex and vague constructs, which makes concluding about the mechanisms underlying change in these cognitive abilities unfounded yet. The conclusions of other narrative reviews are divided on the effectiveness of WM training. For instance, Klingberg (2010) and Morrison and Chein (2011) both see WM training as a promising tool to increase cognitive performance. Melby-Lervåg and Hulme (2013) and Shipstead, Redick and Engle (2010) explain this variance in conclusions by the inconsistencies in results and the used methodology of both the individual reviewed studies as well as the inclusion of studies in reviews.

Preconditions of working memory training

Due to divergent methods it is difficult to draw a general conclusion about the efficacy of WM training or the essential components in a WM training design. Areas of divergence in experimental procedures include: the timeline of training and assessments (e.g., length of training sessions, overall duration of training period, number of assessment sessions), conditions of assessment (e.g., comfort and location of assessment, encouragement level by lab staff), setting of training (e.g., laboratory, school, home), and the particular control groups that are used. These variables can have a profound impact on training outcomes. In spite of this variety in procedures several preconditions for a good

WM training and the valid measurement of its effects have been attempted to formulate. For a valid measurement of transfer abilities of the WM the use of multiple overlapping measurements that differ from the training method is recommended. Jaeggi et al. (2008) used only one task as their transfer variable, which furthermore, required the exact same skill as practiced in the WM training. This lack of multiple measures causes a problematic interpretation of the result. Nevertheless, a study of Schmiedek et al. (2010) has demonstrated far transfer from WM training to fluid intelligence using multiple indices of this variable. Another precondition is the use of an active control group (Shipstead, Redick, & Engle, 2012) with double blind randomization. However, even when the design includes an active control group a placebo effect or a detrimental effect of the experimental condition can influence the results. The experimental group, for instance, often engages in more mentally taxing activities, what might affect their effort either negatively or positively during the post-measurement. Another effect might be that the control group becomes bored or think they are in the control group and thus become less motivated on the post-test.

A precondition which is based on consistent findings in WM training studies is that the effect is most prominent when the training lasts at least 3 weeks or 8 hours (Klingberg, 2010). This is reflected in neuroimaging results, which show that less than 3 hours of WM training resulted in decreased brain activity, whereas studies with longer periods of training showed a mixture of increases and decreases in different brain areas[1]. Despite these mixed results the majority of studies show that a longer training period is essential for achieving the intended effects of WM training. A very important precondition is the adaptivity of the training to the level of the participant (Li et al., 2008; Schmiedek et al., 2010). For instance, easy tasks do not lead to improvement (Takeuchi, Taki, & Kawashima, 2010) because they do not require participants' full engagement and do not control participants' attention, what permit rumination and mind wandering (Hertel, 1998, 2004). Furthermore, depressed individuals' results improve under distraction conditions, converging with the performance of healthy controls (Foulds, 1952). However, two factors concerning training level can

[1] A possible explanation for these mixed results might be that increases in capacity are positively correlated with activity in the intraparietal cortex, middle and superior frontal gyri and caudate nucleus, but that this effect co-occurs with, and can sometimes be dominated by, activity decreases related to learning of strategies, priming during encoding and time-on-task effects.

prevent improvement of WM training. Firstly, a too difficult level may lead to frustration and thus diminished improvement (Klingberg, 2010; Morrison & Chein, 2011). Secondly, automation or the use of strategies decreases the training effect as the task does not challenge WM anymore. Thus, a challenging training which level is adaptive to the individuals' WMC has the most effect.

Redick and colleagues (2013) took all these preconditions into account and explored the effect of WM training in a group of young adults on multiple measures of fluid intelligence, multitasking, WMC, crystallized intelligence, and perceptual speed compared to a no-contact control group and an active placebo-control group. Unless practice effects and a high level of statistical power, WM training did not lead to transfer on any of the cognitive abilities. In sum, results regarding the effect of WM training are very inconsistent. The possibilities and efficiency of this computerized therapy can be very promising but have to be explored thoroughly. In the current dissertation we aimed to examine the effect of WM training in clinical and non-clinical samples with a variety of trainings and measures, to research the efficacy of WM training as valid as possible.

Outline of the current dissertation

This dissertation examines whether increasing WMC by training is able to reduce the negative consequences of WM deficits. In chapter 2, we first investigated whether a high WMC can protect against depressive feelings and a negative interpretation bias. To explore this question, students with a high and low WMC received a high or low WM load. After loading their WM they received questionnaires and tasks measuring their mood and interpretation bias. In other words, we measured whether pushing one's WM to the limit would result in a negative mood state. Chapters 3 to 7 investigate the effect of WM training on WMC, psychopathology and related substrates, stress, coping, self- and attentional control, impulsivity, and academic performance. This question was explored by comparing a group that received a WM training that adapted to their WMC with one that was exposed to a placebo training. We expected a WM training would increase WMC and accordingly, improve related behavior. Specifically, chapter 3 explores whether WM training in individuals with a current depressive episode or anxiety disorder results in an increased WM and reduction in symptoms of depression, anxiety, and rumination. Chapter 4 used a self-

designed WM training and explored the result of training on the same measures and in individuals with the same diagnoses as chapter 3, with a focus on rumination. Chapter 5 used the same WM training as chapter 4 but in a population of SUD inpatients. We measured whether training their WM would reduce their substance use, craving, impulsivity, attention bias, anxiety and depression. Chapter 6 focuses on a healthy student population. Two weeks of WM training were expected to lead to an improvement of academic performance, coping and self- and attentional control, and a reduction of stress, impulsivity, intrusions, and anxiety and depression symptoms. Lastly, chapter 7, examined whether a gamified WM training would lead to less depression, anxiety, and rumination in dysphoric students. Moreover, we compared their WMC before and after training with those of healthy students. The discussion and conclusion (chapter 8) summarizes and integrates all results. Furthermore, limitations of the studies, clinical implications and suggestions for future research are addressed.

Chapter 2|

Pushing Working Memory to the Limit: The Influence of Cognitive Load on Mood

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Abstract

Depression and rumination are associated with difficulties in controlling the content of working memory (WM). Furthermore, the level of working memory capacity (WMC) seems to be essential in suppressing and coping with intrusions. In the current study we explored whether a high WMC protects against a sad mood, by manipulating WM load. High and low scoring participants on a WM task were exposed to a high and low WM load and a sad mood induction. No effect of WM load in combination with the level of WMC was found on mood and interpretation bias, nor of WMC solely. However, a high WM load resulted in a larger increase of anxiety and reduction of cheerfulness compared with a low load. These findings suggest that WMC seems not to have an effect on coping with a negative mood in a healthy sample.

Depressed individuals have an inclination to respond to negative mood states and negative life events with ruminative thinking: uncontrollable negative thoughts about the experienced symptoms and situations which in turn interfere with their ability to concentrate and carry out daily activities (Nolen-Hoeksema, 2000). This association between ruminative thinking and depression may be explained by the finding that both rumination and depression involve difficulties in controlling the contents of working memory (WM; e.g. Hertel, 1997; Joormann, 2005). Working memory is part of our memory system and temporarily stores, activates and maintains information. This memory component is responsible for cognitive functions including allocation of attention, planning, strategy selection, reasoning, and learning (see Baddeley, 1992).

It is hypothesized that depression is attributable to a dysfunction of the central executive component of WM that fails in the efficient distribution of processing resources (Channon, Baker, & Robertson, 1993). This dysfunction might be due to diminished functioning of the three key WM processes that are identified by Miyake and colleagues (2000). That is, depressed patients show an inability to inhibit irrelevant information from entering one's WM (Friedman & Miyake, 2004; Hasher, Zacks, & May, 1999), to replace old, no longer relevant information with newer, more relevant information (e.g. Joormann & Gotlib, 2008), and to shift from negative to positive or neutral interpretations of stimuli (Murphy et al., 1999). Most importantly, rumination is related to deficits in these three WM key processes (Joorman, Nee, Berman, Jonides, & Gotlib, 2010; Whitmer & Banich, 2007).

There is some evidence that depressed individuals have indeed difficulties in typical WM functions (Ilkowska & Engle, 2010) like, learning, attention (Zakzanis, Leach, & Kaplan, 1998), decision-making (Murphy et al., 2001), and planning (Elliott et al., 1996). Structural (Soares & Mann, 1997) and functional neuroimaging (Elliott et al., 1996; Okada, Okamoto, Morinobu, Yamawaki, & Yokota, 2003; Videbech et al., 2002) research confirms the central role of these dysfunctional WM processes in depression as putative WM brain regions. That is, the dorsolateral prefrontal cortex (PFC) and anterior cingulate cortex, are shown to have deficits in depressed patients.

As WM seems to play a role in the onset and maintenance of depression and rumination, a significant question is whether a high WMC may *protect* against symptoms of depression. Indeed, individuals high in WMC have been found to suppress and to cope with intrusions better than individuals low in WMC (Unsworth & Engle, 2007). This is caused by better inhibitory control, an important WM function (Hasher, Lustig, & Zacks, 2007). Both intrusions (Reynolds & Brewin, 1999) and decreased suppression abilities (Howell & Conway, 1992) play a significant role in depression. The suppression of negative thoughts thus requires an adequate WM performance. This process costs even more effort when WM is loaded, especially in people low in WMC (Barrett, Tugade, & Engle, 2004). When WM functions do not work adequately or are too heavily loaded it falls short to suppress these negative thoughts. This can result in the surface of depressive cognitions and the unmasking of the vulnerability to depression, which potentially lead to a depressive episode (Wenzlaff & Bates, 1998).

To our knowledge no experimental study has examined the effect of WMC on mood, by manipulating WM load. In the current study we investigated this effect by randomly exposing students with high vs. low WMC to a high vs. low WM load condition. We provoked a sad mood by a negative mood induction (Seibert & Ellis, 1991). We predicted students with a low WMC that were exposed to a high WM load would be sadder and interpret ambiguous scenarios in a more negative way than the other three groups. Furthermore, as we manipulated the WM load between the two conditions, this should be reflected in significant different short-term memory (STM) test scores. WM and STM are closely related concepts, so when one's WM is highly loaded, their STM would execute less efficiently (Engle, Tuholski, Laughlin, & Conway, 1999).

Moreover, we measured subjects' ability to recall specific autobiographical memories, since depressed individuals have difficulties with that and this ability is a good predictor of a depressive episode (Williams et al., 2007). We hypothesized that participants with a low WMC who were exposed to a high WM load would recall less specific autobiographical memories, because the negative mood induction had the strongest effect in this group. By investigating the current research question we attempt to further explore the role of WM in depressive feelings.

Method

Participants and procedure

Figure 1 (see appendix A) shows the procedure and measures of the experiment, which was executed in the psychological laboratory of the Erasmus University Rotterdam, the Netherlands. Two hundred thirty-seven students of the Erasmus University Rotterdam participated for course credits. The first part of the experiment consisted of measures assessing WM and psychopathology. Fifty participants were removed from the sample due to failure to maintain our 80% accuracy criterion on the sentences part of the Reading Span. A large amount of errors in this part of the task suggests participants did not read and judge the sentences seriously. From the 187 remaining students, participants in the 35% highest and 35% lowest WMC were tested again in the second part of the study. The second part of the study took place after a couple of months and partly, due to a small sample size, after two years. All participants had to execute the Reading Span again and could participate when their score still fell in the same group: 35% highest or lowest scoring participants. WMC was measured by the Reading Span score, which is the sum of letters in perfectly recalled sets. In the second part of the study participants in both groups were randomly assigned to the low or high WM load condition. Thus, four groups were formed; 1) students with a high WMC in the high WM load condition, 2) high WMC and low WM load, 3) low WMC and high WM load and 4) low WMC and low WM load. In part 2 we measured the effect of cognitive load on mood, STM and autobiographical memory specificity. To measure the effect of the cognitive load manipulation on response to a mood induction, participants were required to respond to ambiguous scenarios. The order of the two STM tasks and the three WM tasks was counterbalanced.

Materials and measures

Part 1

Reading span. The Reading Span (Daneman & Carpenter, 1980) tests the processing and storage functions of the WM. Participants need to switch between two tasks; memorize a set of letters and judge the meaning of a sentence as correct or incorrect (e.g. "Andy was stopped by the policeman because he crossed the yellow heaven"). The sets range from 3 to 7 letters and, each of these levels randomly repeats for 3 times. To make sure participants focus on both parts of the task the goal is to judge 85 percent of the sentences

correctly. The sum of letters in all totally correct recalled sets was used for the analysis. The psychometric properties of this task are satisfactory (Conway et al., 2005).

Digit span. The forward Digit Span (Lumley & Calhoun, 1934) is a frequently used measure for STM, while the backward condition measures WM. Participants are instructed to recall a string of digits, respectively forwards (*range* 3 – 12) and backwards (*range* 2 – 10). After correct recall the level of the task increases while an incorrect answer leads to repetition of the level. The level decreases after two adjacent incorrect answers. The traditional score, which is the score before two adjacent incorrect responses are made was measured in this task. The psychometric properties of this task are described as good (Kane et al., 2004).

Beck Depression Inventory – II (BDI-II). The BDI – II (Beck, Steer, & Brown, 1996; Dutch version: Van der Does, 2002) measures depression symptoms. This self-report questionnaire contains 21 groups of statements about different behavioral themes. The option of the group that fits most appropriately the mood of the last two weeks must be selected, with scores ranging from 0 to 3. The total score is calculated by adding up the scores of the questions. This test is widely used and has good psychometric values (Evers, Vliet-Mulder, & Groot, 2005) with a Cronbach's α of .89 in the present study.

State-Trait Anxiety Inventory (STAI). The STAI (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983; Dutch version: Van der Ploeg, Defares & Spielberger, 1980) measures self-reported state and trait anxiety. Both subscales consist of 20 items, with the state-scale measuring transient anxiety and the trait-scale dispositional anxiety. Both subscale scores were used in the current analyses, which are the sum of item scores ranging from 1 to 4. The psychometric qualities of this questionnaire are good (Bieling, Antony & Swinson, 1998), with a Cronbach's α of .93 for the STAI trait as well as for the STAI state in the present study.

Visual Analogue Scale (VAS). To measure their emotional state participants rated their mood states (sad, anxious, cheerful, relaxed and angry) on a digital ruler from 0 to 100.

Part 2

In part two, all participants executed the BDI-II, STAI and VAS again - and the measures and tasks below.

Utrecht Coping List (UCL). The UCL (Schreurs, van de Willige, Tellegen, & Brosschot, 1993) is a coping questionnaire that consists of 47 items that are divided on 7 scales of different coping styles, which are; tackling problems actively, palliative reaction, avoidance, expressive support-seeking coping, passive coping, expression of emotions/anger, and comforting cognitions. Answer options consist of a 4-point Likert scale. Research on the psychometric properties of the UCL has been generally favourable (Sanderman & Ormel, 1992). Cronbach's α in this study ranged from .48 to .80.

Depression Adjective Checklist (DAC). The DAC (Lubin, 1965; Dutch version: Arrindell & Van Rooijen, 1999) was used as another measure of depression. Participants have to indicate whether the 34 words, that reflect feelings or emotions, are applicable to them. The total score was used (*range* 0 – 34), which is the total amount of applicable words in the dysphoric scale (22 words) and non-applicable words in the euphoric scale (12 words). The psychometric values of this test are good (Van Rooijen & Arrindell, 1987).

Symmetry Span. The Symmetry Span (Kane et al., 2004) is often used to measure shifting between attention and spatial WM. Participants have to remember the location and order of red squares in a 4 by 4 grid, while they have to judge figures on an 8 by 8 matrix on vertical symmetry. The easy condition consisted of 21 trials of 2 squares, alternated with figures, while the difficult condition had 5 times 5 and 3 times 6 a combination of squares and figures. To assure the focus of participants on both parts of the task participants were urged to judge at least 85 percent of the figures correctly. In this study the partial-credit unit (PCU) scoring was used (Conway et al., 2005); the percentage correctly recalled items. This task shows good internal reliability (Kane et al., 2004).

Operation Span. The Operation Span (Unsworth, Heitz, Schrock, & Engle, 2005) is one of the most used WM tasks (Conway et al., 2005) and measures shifting and updating WM abilities. Participants have to remember letters, while they solve math problems. The easy

condition consisted of 38 trials of 2 letters that are alternated with math problems, while the difficult condition entailed 5 times 5 and 6 times 7 of these combinations. To assure the focus of participants on both parts of the task the goal was to judge 85 percent of the math problems correctly. The partial-credit unit (PCU) scoring was used in the analyses (Conway et al., 2005); the percentage correctly recalled items. The test shows good internal consistency and test–retest reliability (Conway et al., 2005).

Running Span. During the Running Span (Pollack, Johnson, & Knaff, 1959) subjects watch a string of letters of unknown length and need to recall a specific number of these items in serial order. In the difficult condition participants randomly received strings varying from 3 to 8 items, the number of letters to be recalled was maximal 2 letters less than the length of the string. In the easy condition subjects had to remember 2 letters of a 3-item string. In this study the partial-credit unit (PCU) scoring was used (Broadway & Engle, 2010). The Running Span is an extensively used method to measure inhibition and updating abilities and is found to be a valid measure of WM (Broadway & Engle, 2010).

Mood induction. An adapted version of the mood induction of Seibert and Ellis (1991), which itself is a modified version of Velten's mood induction (1968), was used. To induce a depressive mood, participants saw 25 sentences (Richell & Anderson, 2004) with a sad content for 45 seconds each. Participants were instructed to read the sentence aloud and try to feel and experience like the sentence was applicable to them. During the task participants heard "Russia under the Mongol yoke" from Profkiev. After the mood induction participants had to read 11 ambiguous situations and write down their initial thoughts. Responses were scored as 1 (*very negative*), 2 (*negative*), 3 (*neutral*), and 4 (*positive*). The number of scores in each category and the total score were used in this study. Hereafter they had to rate the probability of a neutral, positive and negative scenario on a 0 to 100 scale. The sum of scores of each 'type' of scenario was used in the analyses. Situations and scenarios were based on Lawson and MacLeod (1999). Good interrater agreement was shown (K = .93) in the current study.

Sentence Completion for Events from the Past Test (SCEPT). The SCEPT (Raes, Hermans, Williams, & Eelen, 2007) is a measure for overgeneral memory in non-clinical populations.

The eleven items consist of half sentences that need to be finished with the first memory that comes up. Responses were coded as a specific memory, categorical memory, extended memory, semantic associate, and omission. The total amount of responses in these categories was analyzed in this study. Good interrater agreement was shown (K = .81) in the current study.

Analyses

Group differences: Psychopathology and IQ

Analyses of variance (ANOVAs) were used for normally distributed data while the Kruskal Wallis test was used for non-normally distributed data. The four groups (low vs. high WMC in combination with low vs. high WM load condition) did not differ on the BDI-II (H (3) = 3.16, p >.05, *partial* η^2 = .04), STAI state (F (3, 79) = 0.23, p > .05, ω^2 = .17), STAI trait (H (3) = 3.54, p >.05, *partial* η^2 = .04), UCL avoidance (F (3, 79) = 0.35, p > .05, ω^2 = .16), UCL support seeking (F (3, 79) = 1.89, p > .05, ω^2 = .18) and any of the other UCL subscales (all H (3) < 5.87, p >.05, *partial* η^2 < .07). Unexpectedly, the groups did differ on the UCL comforting cognitions (F (3, 79) = 2.82, p < .05, ω^2 = .25). However, this significant result disappeared when applying contrasts. Nor did the groups differ on IQ (H (3) = 5.06, p >.05, *partial* η^2 = .06).

WM load manipulation check: SS, OS, RS

Results of a two-way WM load condition x WMC ANOVA show that the WM load manipulation worked as intended. That is, the manipulation in WM load led to different effects in individuals with a high and those with a low WMC on the Symmetry Span (F (1, 76) = 4.56, p < .05, ω^2 = .01), Operation Span (F (1, 78) = 20.10, p < .001, ω^2 = .09), and the Running Span (F (1, 77) = 25.06, p < .001, ω^2 = .09; see Table 1). Simple effects revealed that the WM of individuals with a low WMC functioned worse when under a high WM load, compared to the ones with a high WMC, on the Symmetry Span (F (1, 76) = 13.76, p < .001, r = .39), Operation Span (F (1, 74) = 41.90, p < .001, r = .60), and Running Span (F (1, 77) = 57.00, p < .001, r = .65). In contrast, when the WM load was low, the level of WMC had no effect on the Symmetry Span (F (1, 76) = 0.40, p > .05, r = .07), Operation Span (F (1, 74) = 0.10, p > .05, r = .04), and Running Span scores (F (1, 77) = 0.11, p > .05, r = .04). These results

show that the level of WMC had no effect on performance when under low WM load, but it did manifest in different performance when WMC was pushed to the limit.

Table 1. Mean (and standard deviation) of the four groups on working memory tests

	Low WM load		High WM load	
	Low WMC	High WMC	Low WMC	High WMC
SS	.91 (.07)	.94 (.06)	.39 (.18)	.54 (.17)
OS	.96 (.04)	.98 (.02)	.44 (.23)	.75 (.18)
RS	.98 (.03)	1.00 (.01)	.45 (.18)	.73 (.15)

Note: SS = Symmetry Span, OS = Operation Span, RS = Reading Span

Short term memory: Digit Span

We expected that a loaded WM would affect STM, measured with the Digit Span before and after the WM load manipulation. To analyze the effect we used a RM ANOVA with WM load and level of WMC as between subject factors and the two Digit Span measurements as within subject factor. Unexpectedly, no interaction effect of WM load condition x WMC was found for the Digit Span (Forward: F (1, 81) = 0.14, p > .05, *partial* η^2 = .00, Backward: F (1, 79) = 0.18, p > .05, *partial* η^2 = .00). The level of WMC did not lead to differences in STM performance (Forward: F (1, 81) = 0.05, p > .05, *partial* η^2 = .00, Backward: F (1, 79) = 3.98, p > .05, *partial* η^2 = .05). Neither did the WM load influence the performance on this task (Forward: F (1, 81) = 0.14, p > .05, *partial* η^2 = .00, Backward: F (1, 79) = 0.02, p > .05, *partial* η^2 = .00). Overall, we found no difference between the first and second Digit Span (Forward: F (1, 81) = 0.05, p > .05, *partial* η^2 = .00, Backward: F (1, 79) = 0.63, p > .05, *partial* η^2 = .01). Thus, loading the WM did not affect the performance of STM.

Depression: DAC

To analyze the effect of the WM load and mood manipulation on depression we used a RM ANOVA with WM load and level of WMC as between subject factors and the two DAC measurements as within subject factor. Unexpectedly, the WM load condition x WMC manipulation caused no significant interaction effect on the two measurements of the DAC (F (1, 75) = 0.40, p > .05, *partial* η^2 = .01). Nor, main effects were found for WMC (F (1, 75) = 1.79, p > .05, *partial* η^2 = .02), or WM load condition (F (1, 75) = 0.01, p > .05, *partial* η^2 = .00).

However, a significant time effect reflected that participants felt more depressed after (M = 12.73, Sd = 5.65) than before (M = 7.65, Sd = 6.63) the WM load manipulation and mood induction (F (1, 75) = 62.93, p < .001, *partial* η^2 = .46).

Mood states: VAS sad, anxious, cheerful, relaxed, and angry

To assess the effect of the WM load manipulation on participants' emotional state, we used a 2 WM load condition (low vs. high WM load) x 2 WMC level (low vs. high WMC) repeated measures ANOVA for the four different VAS measurements[2]. Greenhouse-Geisser adjustments were used under violations of sphericity[3]. Against expectations, no interaction effect of WM load condition x WMC was found on any of the different VAS measures (see Table 2 in appendix B). In addition, the level of WMC did not influence participants' mood. In other words, the low and high WMC groups did not differ on any VAS measurement. However, the level of the WM load had a significant effect on their anxiety and cheerfulness (see Table 3 in appendix C). That is, contrasts showed that on average participants in the low WM load condition were more anxious than the ones in the high WM load condition before the WM load manipulation. This pattern of results was reversed after the WM load manipulation (F (1, 68) = 6.98, p < .05, r = .31). Thus, a high WM load directly provoked more anxiety than a low WM load. The results on the anxiety VAS was in line with the results on the VAS which measured cheerfulness. Contrasts revealed that on average participants in the low and high WM load condition were almost as cheerful before the WM load manipulation, but participants in the high load condition became less cheerful after the WM tasks compared with the low load condition (F (1, 68) = 12.89, p < .01, r = .40). In sum, as expected a high WM load affected some of participants' emotional states more than a low WM load did. However, the hypothesized manifestation of WMC on mood, as a result of WM load, was absent.

As intended, significant contrasts on all VAS scales except anxiety revealed that participants became more sad (F (1, 68) = 43.04, p < .001, r = .62), less cheerful (F (1, 68) = 25.07, p < .001, r = .52), less relaxed (F (1, 68) = 13.68, p < .001, r = .41), and more angry (F (1,

[2] This article only describes the relevant analyses for answering the hypotheses. Extended analyses can be requested from the first author.
[3] Details of Greenhouse-Geisser analyses can be asked for by the first author.

68) = 7.44, $p < .01$, $r = .31$) due to the mood induction. Taken together, the mood induction established the intended significant effect on all the measured emotional states but the effect lasted only briefly.

Ambiguous scenarios

Unexpectedly, the variance in WM load or WMC did not lead to significant different responses to ambiguous scenarios showed by a two-way WM load condition x WMC ANOVA. Specifically, the groups did not differ on the number of very negative responses, the number of negative responses, the number of neutral responses, the number of positive responses, and the total score (all F (1, 83) < 1.71, $p > .05$, $\omega^2 < .00$). For none of these categories significant main effects of WM load condition (all F (1, 83) < 1.24, $p > .05$, $\omega^2 < .00$) or group (all F (1, 83) < 0.16, $p > .05$, $\omega^2 < .00$) were found. Neither an interaction effect was found for the positive, negative and neutral answer options (F (1, 83) < 3.45, $p > .05$, $\omega^2 < .03$). The difference in WM load did not lead to different ratings of scenarios (all F (1, 83) < 1.48, $p > .05$, $\omega^2 < .00$), nor did the difference in WMC (all measures F (1, 83) < 0.14, $p > .05$, $\omega^2 < .00$).

Autobiographical memory specificity: SCEPT

A two-way WM load condition x WMC ANOVA was used to explore the effect of the WM load manipulation on the recall of specific memories in the different groups. The only significant interaction effect found was the number of omissions (F (1, 83) = 7.51, $p < .01$, $\omega^2 = .08$). Simple effects revealed that individuals with a low WMC had more omissions in the high (M = 0.63; Sd = 0.68) than in the low WM load condition (M =0.06; Sd = 0.24) (F (1, 83) = 7.34, $p < .01$ $r = .29$). No significant interaction effects were found in the other categories (all (F (1, 83) < 1.19, $p > .05$, $\omega^2 < .03$). The hypothesized group effect was neither found (all F (1, 83) < 2.24, $p > .05$, $\omega^2 < .01$). The WM load only influenced the number of omissions (F (1, 83) = 4.29, $p < .05$, $\omega^2 = .04$), but none of the other categories (all F (1, 83) < 0.83, $p > .05$, $\omega^2 < .00$).

Discussion and conclusion

The current study examined the consequences of manipulating working memory (WM) load in individuals with low and high working memory capacity (WMC) on mood, interpretation bias, short term memory and the specificity of autobiographical memories. Contrary to our expectations, the current study showed mixed results: despite the finding that the mood induction and WM load manipulation worked as intended it did not lead to a more negative mood in participants with a low WMC who were exposed to a high WM load, compared to participants in the other groups. The results neither showed a stronger interpretation bias or a decreased STM as a consequence of a high WM load in combination with a low WMC. The only significant group effect was that pushing the WM of persons with a low WMC to the limit together with a negative mood induction resulted in more omissions when recalling specific memories. This effect is partly in line with a study of Kuyken and Dalgleish (2011), which showed that WM deficits lead to difficulties retrieving specific memories when in a negative mood state. Participants' fast recovery of a negative mood might explain the absence of effect on other categories of this task.

The lack of effect of the WM load manipulation on mood was against expectation, since other studies show that persons high in WMC are better in suppressing negative emotions (Schmeichel, Volokhov, & Demaree, 2008). The found result is in line with Wessel, Overwijk, Verwoerd and de Vrieze (2008), who found that WMC was not associated with intrusive cognitions. They argued that WMC is too general to be predictive and suggested studying the different WM abilities of updating, shifting, and inhibition. They indeed found that better updating and inhibition were linked to fewer intrusions. These results are corroborated by Goeleven and colleagues (2006) and Joormann (2004), who reported that dysphoric individuals show inhibitory dysfunctions. In further research, WMC should be measured in a way that covers the different WM abilities. In the present study WMC was only based on Reading Span scores, which measures mainly shifting and updating abilities.

The only main effect of WM load was the larger increase of anxiety and reduction of cheerfulness in the high load conditions compared with those exposed to a low load. This result conflicts with studies showing a highly loaded WM disrupts emotional processing,

like experiencing feelings of anxiety or sadness (Hertel, 1998; Joormann et al., 2010; King & Schaefer, 2011). A possible explanation of the current result is that participants became more anxious and less cheerful because they had to execute three difficult WM tasks instead of one task, like in the mentioned studies.

Unexpectedly, WM load did not lead to the expected decrease of STM in persons with a low WMC who were exposed to a high WM load. The reason for this hypothesis was the close relation between STM and WM (Engle et al., 1999). This means a high WM load costs attention resources (Barrett et al., 2004) and less of the resources is left to perform on the STM task. It might be possible that the Digit Span (DS) was not a good measure to capture this effect. However, the DS shows a relatively high correlation with WM tasks (Dobbs & Rule, 1989). Nevertheless, a limitation in this study was that participants' STM was only measured directly after the WM load manipulation and not after the dysphoric mood induction. It is possible that the negative mood induction was needed to find an effect on STM, because depressed individuals show a decreased STM (Beats et al., 1996; Porter, et al., 2003; Ravnkilde et al., 2002) and their intrusions capture WM (Wessel et al., 2008, Williams et al., 2007). Future studies should take this limitation into account by measuring STM not only after the WM load manipulation but also after the mood induction.

Against expectations, the WM manipulation in combination with the mood induction had no consequences for the interpretation bias of one of the groups. This result is contrary to the majority of studies, which show that people with a low WMC have more difficulties inhibiting negative thoughts (Unsworth & Engle, 2007) – like we provoked in this study with the mood induction – and thus interpret ambiguous scenarios more negatively. An explanation for the lack of effect might be that the effectiveness of the mood induction is somewhat controversial, despite the fact that is the most widely used method (Westermann, Spies, Stahl, & Hesse, 1996). One of the criticisms is that demand characteristics cause a reported mood change instead of an intrinsic change of mood (Buchwald, Strack, & Coyne 1981; Polivy & Doyle, 1980). The finding that effect sizes were larger in studies in which the aim of the mood induction was told to participants than in studies were deception was employed (Westermann et al., 1996) confirm this criticism.

Another explanation of our null findings is that our hypotheses were based on the assumption that a low WMC would lead to a negative mood. Although the majority of studies show an association between a negative mood and low WMC, empirical evidence is inconsistent. For example, Grant, Thase and Sweeney (2001) concluded there were only small WM deficits in depressed outpatients. This result is in line with studies of Fossati, Amar, Raoux, Ergis and Allilaire (1999) and Barch, Sheline, Csernansky and Snyder (2003), which found no differences in WM deficits between young depressed patients and healthy controls. These cognitive deficits may be more severe in older people with major depression, however, especially if they are hospitalized or their depression is chronic (Beats et al., 1996; Palmer et al., 1996). As our sample consisted of students, this might be the cause of our null results. Furthermore, the small sample size of this study might have influenced the effect as this results in low power. Future research has to focus on participant and task characteristics that are determinative in the expression of WM deficits and should use a larger sample.

Several other limitations to this study need to be acknowledged. Firstly, since our participants had low depression scores, we used a mood induction to explore the influence of a dysphoric mood state on the WM load in individuals differing in WMC. A mood induction cannot imitate a real depressed mood. Therefore, to measure the real effect of WM load on mood future studies might study depressed patients instead of healthy students. Secondly, we used no positive mood induction to recover participants' mood. As this was a student population with low scores on depression and anxiety measures, we thought the influence of a positive mood induction would not compensate for the time the induction would take. The results indeed reflect their ability to recover fast from a negative mood state. That is, they were almost as cheerful and relaxed on the last measurement as on the first. For ethical reasons participants can be exposed to a positive mood induction in future studies.

In conclusion, this study failed to find that persons with a high WMC are better able to cope with negative emotions when under high cognitive load than persons low in WMC. This finding is in contrast with previous studies that indicate that a high WMC enables individuals to cope more effectively with negative cognitions (Unsworth & Engle, 2007) and

that cognitive load leads to more depressive cognitions (Wenzlaff & Bates, 1998). Future research is needed to conclude with more certainty whether and in which extent WMC is involved in negative mood states, like depression.

Appendix A

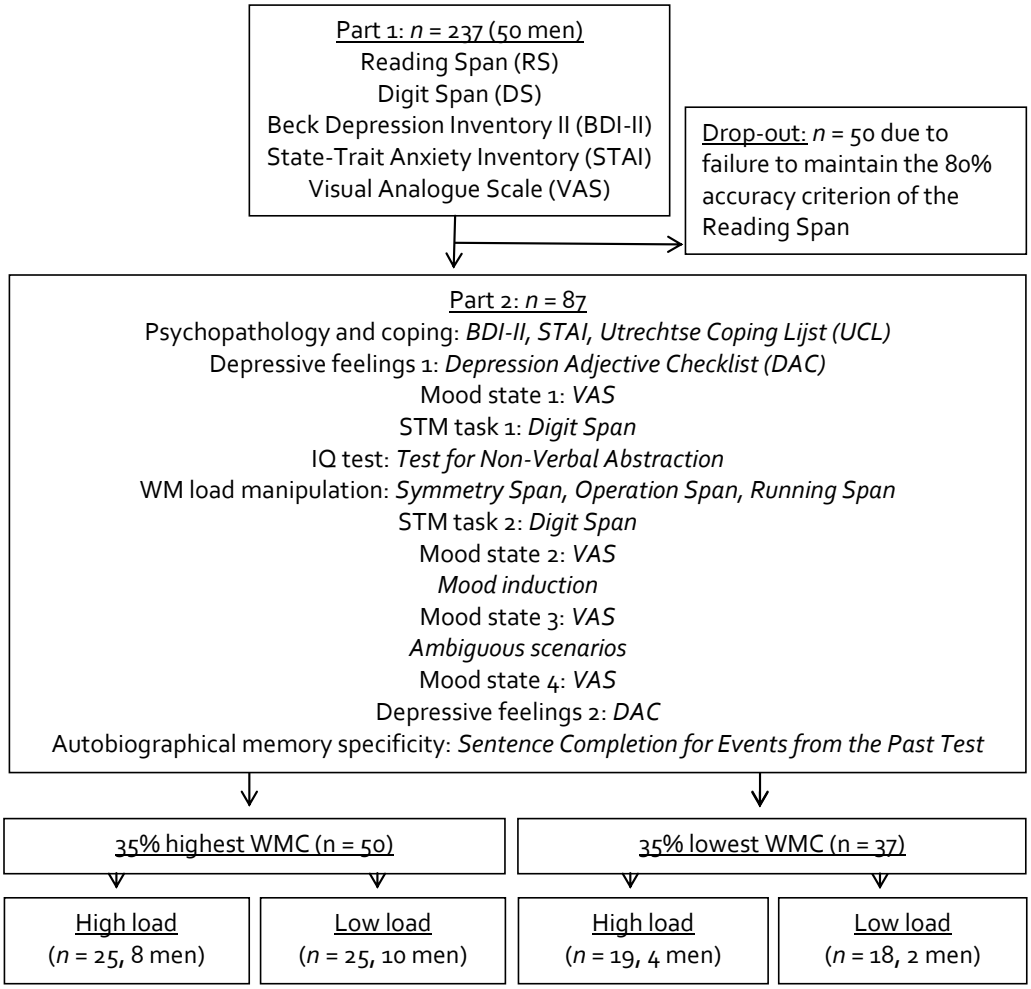

Figure 1. Test procedure

Appendix B

Table 2. Interaction and main effects of wm load, wmc and time on the different vas scales

	Sad (*df* 2.39, 162.45)	Anxious (*df* 1.98, 134.81)	Cheerful (*df* 2.56, 174.17)	Relaxed (*df* 3, 204)	Angry (*df* 2.39, 162.18)
	F	*F*	*F*	*F*	*F*
WM load X WMC	2.02	0.13	1.20	1.97	0.67
WM load	2.76	3.42·	4.20·	1.40	0.19
WMC	1.71	0.60	0.88	0.51	0.60
Time	24.93*	1.91	20.72*	11.41*	4.30·

Note: * Significant at $p < .01$, · significant at $p < .05$

Appendix C

Table 3. Mean (and standard deviation) of the different VAS measurements of the two loads

	Sad		Anxious		Cheerful		Relaxed	Angry		
	Low load	High load	Low load	High load	Low load	High load	Low load	High load	Low load	High load
VAS 1	23.00 (22.12)	21.62 (21.15)	16.41 (25.74)	11.76 (13.39)	55.72 (20.31)	55.88 (18.80)	65.07 (23.71)	66.74 (21.84)	10.93 (17.47)	11.68 (16.75)
VAS 2	14.88 (13.79)	19.28 (19.71)	9.69 (13.75)	12.90 (16.61)	57.85 (18.92)	42.66 (19.44)	67.54 (19.38)	55.79 (19.03)	7.73 (8.35)	10.28 (13.12)
VAS 3	34.73 (24.32)	30.07 (25.11)	13.65 (13.91)	15.79 (17.94)	42.61 (25.56)	36.00 (20.42)	54.15 (27.97)	47.66 (23.21)	15.00 (15.16)	18.38 (17.04)
VAS 4	16.28 (15.77)	25.13 (25.31)	8.38 (12.71)	12.50 (16.01)	57.09 (20.33)	49.71 (17.49)	59.16 (29.36)	59.24 (19.80)	11.28 (16.14)	12.16 (14.26)

Note: VAS 1 = Start of the experiment: before WM load induction, VAS 2 = After WM load induction and before mood induction, VAS 3 = After mood induction, VAS 4 = End of the experiment

Chapter 3|

Effects of Working Memory Training in Depressive and Anxious Patients

This chapter has been submitted for publication as: Wanmaker, S., Geraerts, E., van den Berg, L., Mayer, B., & Koster, E. (submitted). Effects of working memory training in depressive and anxious patients.

Abstract

Anxiety and depression are both associated with impairments in executive functions, including working memory (WM) which is needed to maintain and manipulate goal-relevant information. Due to these WM impairments anxious and depressed individuals have difficulties inhibiting and shifting from irrelevant (negative) information and updating goal relevant information. This study explored whether training WM decreases these impairments and reduces clinical symptoms and rumination. Eighty-four individuals diagnosed with major depression and forty-nine individuals with an anxiety diagnosis executed WM or control tasks three times a week, during four weeks. Before, after training, and at a two months follow-up measurement depression and anxiety symptoms, WM capacity and rumination behaviour were assessed. Training WM did only result in a reduction of anxiety symptoms in the depression sample. These findings are inconsistent with promising results of individual studies showing training WM result in an enlarged WM capacity and a decrease of psychopathological symptoms. However, our results are in line with recent meta-analyses and reviews which show that WM training do not lead to generalized effects and therefore, cast doubt on the clinical relevance of WM training programs.

Both depression (Birrer, Michael, & Munsch, 2007; Nolen-Hoeksema, 2000; Reynolds & Brewin, 1999) and anxiety (Fresco, Frankel, Mennin, Turk, & Heimberg, 2002; Segerstrom, Tsao, Alden, & Craske, 2000) are associated with a tendency to respond with persistent negative thoughts (rumination or worrying) to negative mood states and negative life events (Nolen-Hoeksema, 2000). Empirical evidence confirms the central role of persistent negative thoughts by suggesting that this thinking style is associated with vulnerability to the onset of depression and anxiety disorders. Regarding depression rumination is also related to the recurrence of depressive episodes and the maintenance of a negative mood (Nolen-Hoeksema, 2000). It has been suggested that the cause of these unproductive thoughts might be attributable to deficits in cognitive functions, particularly working memory (WM; Eysenck, 1979, 1982; Eysenck & Calvo, 1992). Patients suffering from depression (e.g. Bishop, 2009; Joormann & Gotlib, 2008) and anxiety (Sorg & Whitney, 1992) indeed show deficits in WM.

WM is a limited-capacity system, responsible for temporary storage, activation, and maintenance of information which is essential for executing a wide range of complex cognitive functions, including reasoning, learning and comprehension (Baddeley, 1992). The WM dysfunction in depressed and anxious patients may explain specific symptoms of these disorders such as problems with concentration, attention, and memory (Chapman & Chapman, 1973, 1978; Ouimet, Gawronski & Dozois, 2009; Weingartner, Cohen, Murphy, Martello, & Gerdt, 1981; Zakzanis, Leach, & Kaplan, 1998). These deficits might not only be a key element in the explanation of both the onset and maintenance of these disorders (Joormann, 2010), but also the cause of the still high relapse rate despite treatment (Bruce et al., 2005; Bystritsky, 2006).

Diminished functioning of all three key WM processes - inhibition, updating and shifting - is related to self-reported rumination (Joormann, Nee, Berman, Jonides, & Gotlib, 2010; Whitmer & Banich, 2007). Moreover, it may be the cause of depressed patients' negativity bias (Blaney, 1986; Levens & Gotlib, 2010; Linville, 1996; Mathews & Mackintosh, 1998; Rusting, 1998). That is, depressed individuals show an impaired ability to inhibit irrelevant information from entering their WM (Lemelin et al., 1996; MacQueen, Tipper, Young, Joffe, & Levitt, 2000; Monsell, 1996; Trichard, et al., 1995). Secondly, depressed

patients are worse in updating their WM than healthy controls, which involves replacing old, no longer relevant information with newer, goal relevant information (Morris & Jones, 1990). In other words, these individuals show greater intrusions from previously relevant negative information when updating their content of WM (Harvey et al., 2004; Joormann & Gotlib, 2008; Whitmer & Banich, 2007). Thirdly, depressed patients show difficulties in directing their attention away from negative information when they are instructed to shift between positive and negative information (Murphy et al., 1999), which underlines their bias for negative stimuli (Nolen-Hoeksema, 2000). In sum, depressed individuals have difficulties controlling the content of their WM, which expresses in rumination. As a result they experience difficulties in repairing their negative mood state (Nolen-Hoeksema, 2000), which may lead to the maintenance of their depressed feelings (Ursin, 2005).

Whereas the majority of studies focused on the relationship between depression and WM, recently the link between anxiety and WM has been studied as well. According to the attentional control theory, anxious individuals' decreased attentional control is a consequence of a disrupted balance in the two attention systems (Corbetta & Shulman, 2002; Eysenck, Derakshan, Santos, & Calvo, 2007). Their decreased attentional control includes problems in shifting back and forth to different mental sets, inhibition of dominant, prepotent responses and, to a lesser degree, updating and monitoring cognitions in WM (Eysenck et al., 2007). Their selective information processing reflects these WM deficits. That is, anxious individuals show a strong attentional bias (Brand & Jolles, 1987; Mathews & MacLeod, 1994) and a tendency to interpret ambiguous information in a negative and threatening way (Amir, Beard, & Bower, 2005; Eysenck, MacLeod, & Mathews, 1987). This focus on threat leads to a continuous stream of threatening information in their WM (Bishop, 2009) and manifests on tasks involving WM or the attentional bias. For instance, anxious individuals show a decreased reaction time on the emotional Stroop task (Mathews & MacLeod, 1985; Watts, McKenna, Sharrock & Trezise, 1986), which exemplifies their decreased inhibition and anxiety-related attentional bias.

As depressed and anxious individuals exhibit WM dysfunctions, the question arises whether training WM may remediate these dysfunctions and the related symptoms. To achieve that goal, a transfer of WM training tasks to general WM functions is needed. Fundamental cognitive research showed that training WM could indeed lead to transfer to other WM tasks (Jaeggi, Buschkuehl, Jonides, & Perrig, 2008). Other studies showed that this transfer is not restricted to transfer tasks but even extends to other cognitive functions, like attention and inhibition (Chein & Morrison, 2010; Klingberg et al., 2002, 2005).

The effect of training WM has been studied in a variety of psychopathological disorders. For example, a WM training showed improved attention, verbal WM, response inhibition, reasoning skills, and decreased hyperactivity in ADHD patients. Interestingly, these training effects persisted for at least six months (Klingberg et al., 2005). Another area is the effect of WM training on alcohol abuse. Houben, Wiers and Jansen (2011) showed that severe drinkers had a reduced alcohol intake for more than one month after training their WM. Importantly, the strength of individuals' automatic impulses moderated the indirect training effect on alcohol intake. That is, individuals with relatively strong automatic preferences for alcohol showed the most reduction of alcohol use as a consequence of WM training. Even individuals with schizophrenia, who intensively trained their WM, perceptual, executive and social cognitive processes, showed improvement in their social functioning, a reduction of their behavioral problems and an increase of their quality of life six months later (Subramaniam et al., 2012). Moreover, training WM may lead to neurological changes (Olesen, Westerberg, & Klingberg, 2004). For instance, a study of McNab et al. (2009) showed that density of cortical dopamine D1 receptors - crucial for WM processes - increased in WM specific areas.

The present study investigated whether training WM in anxious and depressed individuals is able to reduce their clinical symptoms and rumination. Several studies show that cognitive training seems to be a good method to reduce cognitive deficits found in depressed and anxious patients. In a study by Joormann, Hertel, LeMoult and Gotlib (2009) depressed patients learned to use cognitive strategies to inhibit or forget negative information. In addition, Siegle, Ghinassi and Thase (2007) showed that cognitive control

training was a significant addition to the treatment as usual (medication, group and milieu therapy) which led to reduced rumination and depressive symptoms. These results indicate that cognitive control training might help people stop ruminating.

Our WM training consisted of two WM tasks and was compared with a placebo training that consisted of easy versions of these WM training tasks. The importance of a challenging WM training is proven by studies that show that depressed individuals performance is comparable to healthy persons when they execute difficult WM tasks. The high level requires participants to fully engage with the task and controls participants' attention (Channon, Baker, & Robertson, 1993; Foulds, 1952). In other words, the focus of attention shifts from internal cognitive intrusions to task-directed behavior (Krames & MacDonald, 1985).

The primary outcome of this study was the level of depression and transient anxiety symptoms. It is hypothesized that the expected reduction of these symptoms is caused by an increased working memory capacity (WMC), measured by two WM tasks tapping the same WM constructs as the training; shifting, updating and inhibition (secondary outcome measure). Furthermore, we expected rumination would decline, since both WM, depression and anxiety are associated with ruminative thinking (Brewin & Smart, 2005)[4]. In addition, state and total anxiety were tertiary outcome measures, as these measures of stable anxiety are expected to change when there is a strong effect of training WM. Moreover, as the level of anxiety (e.g. Basten, Stelzel & Fiebach, 2011; Bishop, 2009) and depression (e.g. Harvey et al., 2004, Joormann & Gotlib, 2008; Whitmer & Banich, 2007) is related to the extent of WM deficits, we explored whether the anxiety/depression level of participants on the pre-test predicted the effect of the WM training. Both outcomes would be possible: high anxious/depressed individuals profited more from a WM training because they have

[4] Two measures of this study are not described in this article since outcomes were not relevant to answer the research questions described in this article. Firstly, since the ability to recall specific autobiographical memories is negatively correlated with depressive complaints (Williams et al., 2007; Kuyken & Dalgleish, 2011) we measured this with the Autobiographical Memory Test (Williams & Broadbent, 1986). Secondly, to measure participants' ability to cope with a negative or anxious mood after the training we exposed them to a mood induction. Results of both measures were not significant. Detailed information can be asked for by the corresponding author.

more deficits to tackle but these deficits could in turn also decrease the effect of the WM training.

Method

Participants and procedure

The study was conducted in line with the Declaration of Helsinki, approved by the Medical Ethical Committee of the Erasmus University Rotterdam, and registered at ClinicalTrials.gov (ID: NCT02119923). The measurements took place in the laboratory of the Erasmus University Rotterdam. Participants were recruited by several media, including newspapers, television and internet. All participants that subscribed were screened with a short version of the Structured Clinical Interview for the DSM-IV-TR Axis I Disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 1996), to include participants with a current depressive episode and/or anxiety disorder and allocate them to respectively the depression or anxiety study sample. When participants met criteria for both a depression and an anxiety diagnosis, they were allocated to the study of the disorder with the first onset. Participants with a current psychosis or substance dependency and those who exceeded the age range of 16 to 70 years were excluded. Because of the training requirements, participants needed a Windows computer with an Internet Explorer or Firefox browser. Eventually 114 participants were included in the depression sample and 65 in the anxiety sample. Stratified for each group, participants were randomly allocated to the experimental or placebo group, both experimenters and patients were blind for treatment condition (double-blind design). Figures 1 and 2 show the participant flow from the depression and anxiety sample respectively. At the pre-test participants executed the self-report psychopathology questionnaires, two transfer WM tasks and the training and received a booklet with information about the training. Participants were required to execute the training three times a week during four weeks. A training session lasted approximately 25 minutes. The average number of training sessions did not differ between the experimental (M = 11.14, Sd = 2.03) and placebo group (M = 11.24, Sd = 2.41) (U = 789.50, z = -1.09, p > .05, r = -.12) in the depression sample, nor in the anxiety sample (respectively M = 11.93, Sd = 2.82 and M = 11.70, Sd = .95; U = 67.50, z = -.56, p > .05, r = .12). The post- and the follow-up test, which

were respectively scheduled right after the last training session and two months after the post-test, included the same tasks as the pre-test except the training tasks.

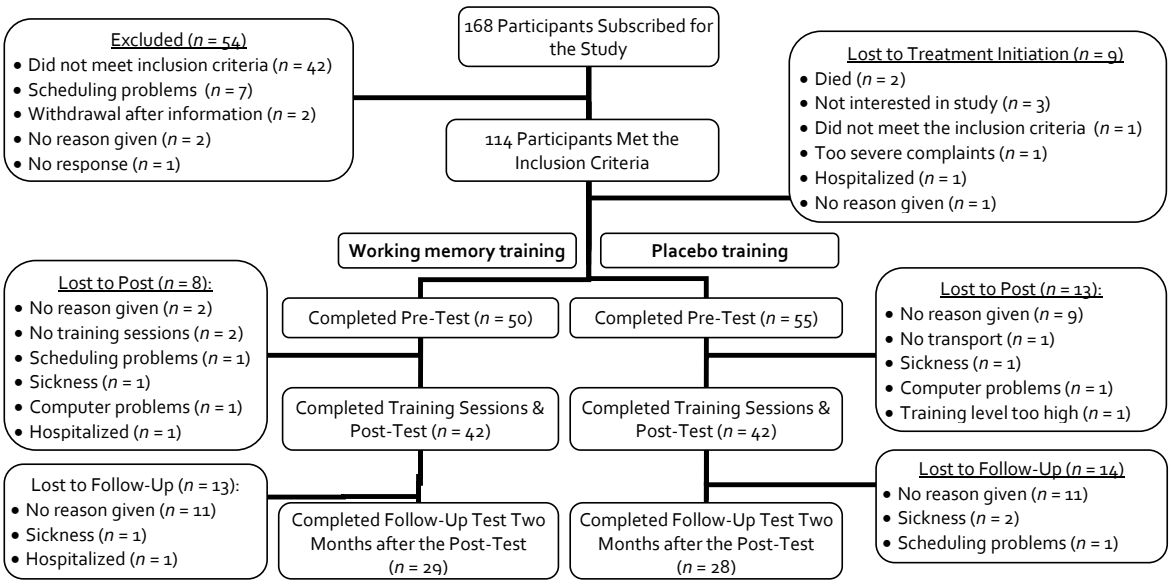

Figure 1. Participant Flow Depression Sample

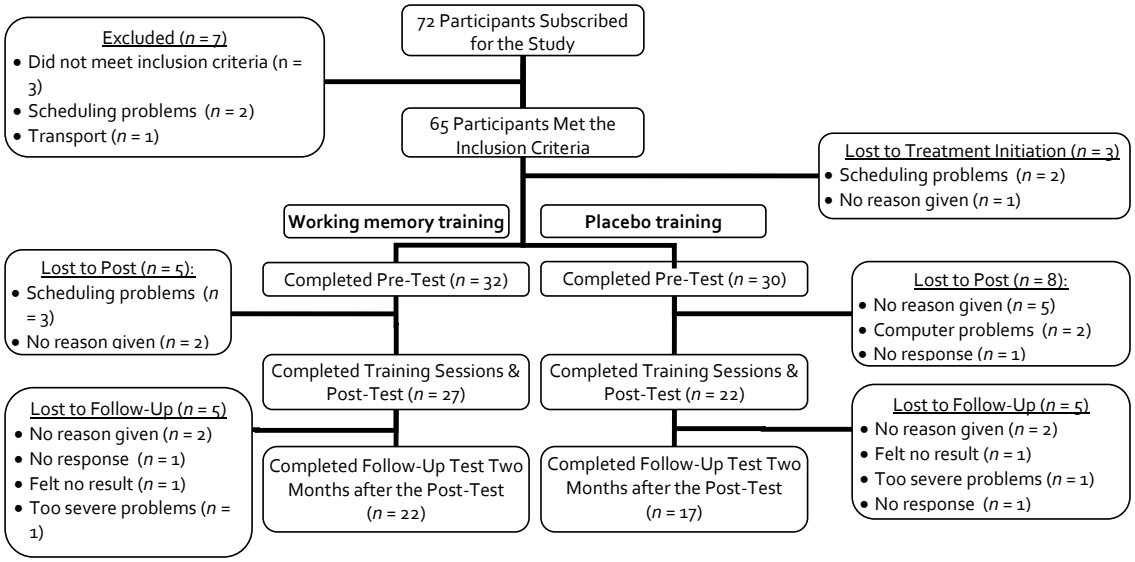

Figure 2. Participant Flow Anxiety Sample

Materials

Assessments

The SCID-I (First et al., 1996; Groenestijn, Akkerhuis, Kupka, Schneider, & Nolen, 1999) was used to screen whether participants met a diagnosis of an anxiety and/or mood disorder. The first author extensively trained the interviewers to administer the SCID-I and supervised them during the screening.

Primary outcome measures. The Dutch version of the Beck Depression Inventory Second Edition (BDI-II: Beck, Steer & Brown, 1996; Van der Does, 2002) was used to measure the severity of depression symptoms. The reliability of this extensively used questionnaire is good (Evers, Vliet-Mulder, & Groot, 2005), with a Cronbach's α of .87 in the present study. This measure was only assessed in the depression study sample.

The trait part of the Dutch version of the State-Trait Anxiety Inventory (STAI: Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983; Van der Ploeg, Defares, & Spielberger, 1979) was assessed as primary outcome measure of anxiety. The psychometric qualities of the STAI are sufficient (Bieling, Antony, & Swinson, 1998), with a Cronbach's α of .81 in the trait part and .92 in the state part in the present study.

Secondary outcome measures. To measure whether the training increased participants' WM they executed two WM tasks - which tapped the same WM constructs as the training - as transfer tasks at the pre and post-measurements. The Internal Shift Task (IST: De Lissnyder, Koster, & De Raedt, 2012) measures participants' ability to shift attention between items stored in WM and the ability to update information stored in WM. The task consists of an emotional and a non-emotional (gender) condition, in which pictures of two categories are presented one by one in the middle of the screen. Participants have to count the number of pictures in each category. The shift costs per condition were used in the analyses, which reflect the effort of shifting attention between the two categories, measured in reaction time (milliseconds). The IST has good reliability and ecological validity (Koster, De Lissnyder, & De Raedt, 2013).

The Symmetry Span (Kane et al., 2004) is a typical WM task in which the participant has to remember the order and location of a set of squares while judging the symmetry of images. Participants are required to recall the location of the squares in correct order at the end of the trial. The task consists of twelve trials, randomly varying in length from two to five items. Previous to the test phase is a practice phase for each task and the combination of both. The partial-credit unit (PCU) scoring was used (Conway et al., 2005), that is the percentage correctly recalled items. The reliability of the Symmetry Span is high (Unsworth, Redick, Heitz, Broadway, & Engle, 2009), with an internal consistency of $\alpha = .86$ (Kane et al., 2004).

Tertiary outcome measures. The Dutch version of the Ruminative Response Scale (RRS; Nolen-Hoeksema & Morrow, 1991; Raes, Hermans, & Eelen, 2003) was used to measure the frequency of self-reported rumination behavior. The questionnaire shows sufficient reliability (Raes et al., 2009), with a Cronbach's α of .89 in the current study. This measure was only assessed in the depression study sample.

The state part and total score of the STAI (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983; Van der Ploeg, Defares, & Spielberger, 1979) were assessed to explore whether training WM had an effect on state and overall anxiety.

Working memory training

Both the WM and the placebo training consisted of two tasks; the Number-letter task (Rogers & Monsell, 1995) and an Updating task. The Number-letter task trains the ability to shift between task relevant stimuli. Participants need to shift between four categories. To prevent training WM the placebo training was a simplified version of the Number-letter task in which shifting was not required. In the Updating task participants receive a set of three words in which they have to compare the two consecutive words on emotional valence (positive or negative) to train their updating skills. To prevent training of their WM the placebo group only had to count the number of positive or negative words.

The duration of a training session was approximately 20 minutes. Participants executed the training three times a week during four weeks. The training was accessible via a website, where they could log in with their subject number. The experiment leaders could monitor the training frequency per participant. To optimize training participation experimenters called participants every week - or earlier when they did not execute the training - to discuss their training participation and mood and motivate them to execute the training.

Apparatus

E-prime (Psychology Software Tools, Pittsburgh, PA) was used for the questionnaires and WM tests. Inquisit (Millisecond, Seattle, WA) was used for the training tasks. For a correct operation of the program participants were required to operate the training on a computer with a Windows 2000, XP, Vista or 7 system and an Internet Explorer or Firefox browser.

Analyses

Data collected on primary measures - depression and anxiety: respectively BDI-II and STAI trait -, secondary measures - WMC: IST and Symmetry Span - as well as tertiary measures - rumination and state and total anxiety: RRS and STAI state and total - were submitted to a two-factor mixed design analyses of variance (ANOVA). Each mixed design ANOVA included one between-subjects factors for group - WM training vs. placebo training - and one within-subject factor for time - pre-training, post-training and follow-up measurement -. Only relevant analyses to answer the research question are reported, that is; interaction effects (Group x Time) and time effects. Extended analyses can be asked for by the corresponding author. In analyses that included more than two within-subjects measurements, Greenhouse-Geisser adjustments were used under violations of sphericity. The significance level was set at .05 for all analyses.

Results

Pre-treatment group differences in depression and anxiety samples

As expected, exact chi-square tests and an independent t-test show that in both samples the experimental and placebo group do not differ on socio-demographic variables (see Table 1 for depression and Table 2 for anxiety sample characteristics).

Table 1. Socio-demographical characteristics of the depression sample

	Working memory training *n* = 42	Placebo training *n* = 42	χ^2 / *t*
% Men	33.3	52.4	$\chi^2 = 3.11$
% Dutch	100	97.6	$\chi^2 = 1.01$
% High education level	52.4	52.4	$\chi^2 = 1.27$
Mean age in years (Std. dev.)	45.69 (12.69)	45.69 (13.27)	$t = .99$
% Use of antidepressants	57.1	59.5	$\chi^2 = .05$
% Use of tranquilizers	0	0	N.a.
% Currently in therapy	47.6	64.3	$\chi^2 = 2.37$
% History of therapy	88.1	81.0	$\chi^2 = .82$
% History of hospital admission	19.0	14.3	$\chi^2 = .34$

Note: N.a. = not applicable; Std. dev. = Standard deviation; High education level = Minimally pre-Bachelor level

Table 2. Socio-demographical characteristics of the anxiety sample

	Working memory training *n* = 27	Placebo training *n* = 22	χ^2 / *t*
% Men	37.0	22.7	χ^2 = 1.17
% Dutch	100	100	N.a.
% High education level	44.4	45.5	χ^2 = 2.81
Mean age in years (Std. dev.)	43.3 (13.42)	48.3 (14.78)	*t* = 1.25
% Use of tranquillizers	18.5	22.7	χ^2 = .13
% Use of antidepressants	40.7	22.7	χ^2 = .18
% Currently in therapy	33.3	36.4	χ^2 = .05
% History of therapy	88.9	90.9	χ^2 = .05
% History of hospital admission	11.1	13.6	χ^2 = .07

Note: N.a. = not applicable; Std. dev. = Standard deviation

Depression sample

Primary measures – Depression and trait anxiety. Unexpectedly, there was no significant interaction effect between the two different conditions for depression on the BDI-II (F (2, 110) = .29, p > .05, *partial* η^2 = .01). However, an interaction effect showed that the two different conditions led to a divergent reduction in anxiety on the STAI trait (F (1.81, 99.47) = 4.73, p < .05, *partial* η^2 = .08). Contrasts revealed that the WM training resulted in a larger reduction of anxiety from the post to follow-up measurement than the placebo training did ((F (1, 55) = 6.98, p < .05, r = .34; see Table 3 in Appendix A). Main effects of time were found on the BDI-II (F (2, 110) = 30.39, p < .001, *partial* η^2 = .36) and on the STAI trait (F (1.81, 99.47) = 107.19, p < .001, *partial* η^2 = .67). Contrasts revealed there was both a significant reduction of depression (F (1, 55) = 56.56, p < .001, r = .71) and trait anxiety between the pre- and post-measurements (F (1, 55) = 12.99, p < .05, r = .44) and between post and follow-up measurements for the STAI trait (F (1, 55) = 86.39, p < .001, r = .78).

Secondary measure – WMC. Contrary to our hypothesis training WM did not lead to an interaction effect between the groups on the IST (global shift costs: F (1.38, 71.77) = 1.33, p >

.05, *partial* η^2 = .02; emotion and gender shift costs, both: F (2, 108) < .44, p > .05, *partial* η^2 = .00) or on the Symmetry Span (F (2, 108) = .23, p > .05, *partial* η^2 = .00). However, a significant main effect of time was found on both emotional shift costs (F (2, 108) = 3.22, p < .05, *partial* η^2 = .06) and the Symmetry Span (F (2, 108) = 3.92, p < .05, *partial* η^2 = .07). Contrasts revealed that on both measures participants performed significantly better on the post measurement (IST: M = 349.63, Sd = 212.62; Symmetry Span: M = .60, Sd = .25) compared with the pre measurement (IST emotional shift costs: M = 423, Sd = 237; Symmetry Span: M = .56, Sd = .26) (IST emotional shift costs: F (1, 54) = 6.53, p < .05, r = .33; Symmetry Span: F (1, 54) = 6.32, p < .05, r = .32). Their improvement on the IST emotional shift costs was a short-term effect, as the scores on the follow-up measurement (M = 399, Sd = 292) were almost significantly higher – meaning a worse performance – than on the post-test (F (1, 54) = 3.38, p = .07, r = .24). The IST global (F (1.38, 71.77) = .16, p > .05, *partial* η^2 = .00) and gender shift costs (F (2, 108) = 1.92, p > .05, *partial* η^2 = .03) did not change over time.

Tertiary measures – Rumination, state and total anxiety. The WM training did neither have an influence on rumination (F (2, 110) = 1.46, p > .05, *partial* η^2 = .03), nor state anxiety (F (1.81, 99.26) = .96, p > .05, *partial* η^2 = .02) compared with the placebo training. However, an interaction effect was found on the STAI total (F (2, 110) = 3.24, p < .05, *partial* η^2 = .06). Contrasts revealed that the WM training resulted in a larger reduction of anxiety from the post to follow-up measurement than the placebo training did ((F (1, 55) = 4.90, p < .05, r = .29; see Table 3 in Appendix A).

Rumination (F (2, 110) = 18.67, p < .001, *partial* η^2 = .25), state (F (1.81, 99.26) = 3.56, p < .05, *partial* η^2 = .06) and total anxiety (F (2, 110) = 38.24, p < .05, *partial* η^2 = .41) all decreased over time across both groups. Participants' rumination (F (1, 55) = 17.72, p < .001, r = .49; see Table 3 in Appendix A), state and total anxiety (both STAI scales (F (1, 55) > 9.14, p < .05, r < .38) decreased after the training, and even less two months after the end of the training (rumination; F (1, 55) = 4.69, p < .05, r = .28 and STAI total; F (1, 55) = 21.11, p < .001, r = .53).

Anxiety sample

Primary measure – Trait anxiety. Unexpectedly, mixed design ANOVAs showed that individuals who executed the WM training did not experience a larger decrease in trait than the placebo training group (F (2, 72) = 1.07, p > .05, *partial* η^2 = .03). However, self-reported trait anxiety reduced in both groups over time (F (2, 72) = 9.56, p < .001, *partial* η^2 = .21). As expected, participants were on average more anxious on the pre-test than on the post-test (F (1, 36) = 13.32, p < .05, r = .52).

Secondary measure – WMC. Surprisingly, the WM training did not lead to transfer to either of the transfer tasks: the IST (global and emotional shift costs both: F (2, 68) < 1.46, p > .05, *partial* η^2 < .04; gender shift costs: F (1.62, 55.21) = .49, p > .05, *partial* η^2 = .01) and the Symmetry Span (F (1.57, 53.37) = 1.51, p > .05, *partial* η^2 = .04). The main effect of time reached significance in the IST (global shift costs: F (2, 68) = 3.38, p < .05, *partial* η^2 = .21; emotional shift costs: F (2, 68) = 43.44, p < .05, *partial* η^2 = .56) and approached significance in the Symmetry Span (F (1.57, 53.37) = 3.18, p = .06, *partial* η^2 = .09). Specifically, significant improvements between the pre and post measurements were found (see Table 4; IST global shift costs: F (1, 34) = 8.79, p < .05, *partial* η^2 = .09; IST emotional shift costs: F (1, 34) = 48.74, p < .001, *partial* η^2 = .59; Symmetry Span: F (1, 34) = 7.18, p < .05, r = .42). Moreover, the emotional shift costs continued to reduce from post to follow-up measurement (F (1, 34) = 100.93, p < .001, *partial* η^2 = .75). However, the gender shift costs did not reduce as a product of time (F (1.62, 55.21) = 1.73, p > .05, *partial* η^2 = .04).

Table 4. Mean (and Standard Deviations) on the IST and Symmetry Span in the anxiety sample

	Pre		Post		Follow-up	
Measurement	WM training	Placebo training	WM training	Placebo training	WM training	Placebo training
IST global shift costs	360 (171)	391 (202)	308 (140)	331 (176)	322 (164)	369 (276)
IST emotional shift costs	379 (149)	345 (254)	122 (91)	168 (130)	341 (173)	390 (222)
IST gender shift costs	350 (242)	409 (203)	319 (167)	339 (181)	291 (169)	372 (327)
Symmetry Span	.59 (.24)	.59 (.25)	.69 (.23)	.61 (.20)	.65 (.24)	.63 (.25)

Tertiary measure – Total and state anxiety. Mixed design ANOVAs showed that individuals who executed the WM training neither experienced a larger decrease in total and state anxiety than the placebo training group (STAI total and state both; F (2, 72) < .34, p > .05, *partial* η^2 < .01. However, self-reported transient anxiety reduced in both groups over time (both STAI scales; F (2, 72) > 4.21, p < .05, *partial* η^2 > .11). As expected, participants were on average more anxious on the pre-test than on the post-test (both STAI scales, F (1, 36) > 5.85, p < .05, r > .37).

Predictors of responding to working memory training effect

To examine whether participants' level of depression and trait anxiety before the training would predict the effect of WM training on depression, anxiety or WMC we executed linear regression analyses using standardized values with the level of their anxiety (STAI trait: both samples combined for a larger power) and depression (BDI-II: only depression sample) symptoms at pre-test as predictors and compared the WM and placebo training. Interestingly, a higher level of trait anxiety on the pre-test predicts a higher decrease of trait anxiety as a result of the training (R^2 = .05, B = .22, p < .05). In contrast, the level of depressive symptoms of the depression sample at pre-test did not predict a difference change in depression during the training between the two groups (R^2 = .09, B = .04, p > .05). The level of self-reported depression or anxiety symptoms on the pre-test did

neither influence the WM ability to shift between emotional stimuli, measured with the IST emotional shift (all $R^2 < .02$, $B < .06$, $p > .05$), nor the coping with interference, measured with the Symmetry Span ($R^2 < .01$, $B < .09$, $p > .05$).

Discussion and conclusion

This study explored whether a WM training may be able to reduce anxiety and depression symptoms in depressed and anxious participants by increasing their WMC. As expected, training WM resulted in a reduction of trait anxiety symptoms. However, this effect only occurred in the depression group. Important for the interpretation of that effect is the significant higher trait anxiety of the depression sample (M = 60.92, Sd = 8.33) compared to the anxiety sample (M = 54.25, Sd = 5.79; t (124.98) = -5.40, $p < .001$, r = .44). The finding that a higher level of trait anxiety before the training is predictive for a larger decrease of trait anxiety as a result of the training, confirms the effect of this WM training on anxiety. Unexpectedly, the training did not reduce depressive symptoms in depressed individuals, neither rumination nor anxiety in the anxiety sample.

This study is the first study which shows the effect of WM training on anxiety in a sample suffering from an anxiety disorder. Important to note is that the largest effect was found in high anxious persons. Future research has to reveal whether a WM training will be a practical tool for clinical use. Surprisingly, these effects are found while WMC was not increased. This lack of transfer of the WM training to other WM tasks might explain the absence of the training effect on state anxiety, depression and rumination. This result is in line with other studies that did not find near transfer effects (e.g., Onraedt & Koster, 2014). Surprisingly, in the absence of a near transfer effect some of these studies found far transfer effects of WM training to fluid intelligence (Jaeggi et al., 2008; Jaeggi et al., 2010). However, this is a controversial finding since a far transfer effect without a near transfer effect is difficult to interpret (Melby-Lervåg & Hulme, 2013). In the current study only a practice effect of the WM tasks was found, as participants - across all groups - had all improved scores on the WM tasks on the second measurement. An effect of time also appeared on the level of self-reported depression, anxiety, and rumination symptoms of depressed individuals and anxiety symptoms of anxious individuals. The reduction of psychopathology over time is in line with studies that showed depression and anxiety

decrease over time (Kruijshaar et al., 2005; Ramsawh, Raffa, Edelen, Rende, & Keller, 2009; Spijker et al., 2002). Another cause for the comparable effect of the placebo and experimental training might be that both resulted in a comparable increased WMC. However, as the placebo training was very easy, the option that this would have led to an increased WMC is improbable.

The results might be influenced by a number of limitations in the current study. Firstly, the WM tasks that were used in the training were based on other WM tasks but this was the first time they were implemented in a WM training for this population. This limitation points to one of the main issues in WM training studies. As a large variety of factors can influence the results, including training tasks, length and duration of training, population and transfer tasks, it is difficult to draw conclusions about the effectiveness of WM training in general. Provided some encouraging findings in subclinical (e.g., Owens, Koster, & Derakshan, 2013) and clinical samples (Iaccovelli et al. in press) it is important to examine under which conditions training works. Our paper is important in further understanding which particular method of training is effective.

The second limitation concerns the recruitment of the study sample, by means of several media, which could have influenced participant' characteristics. Our depression sample was on average older (Van 't Land, Schoemaker, & de Ruiter, 2008) and in both samples high-educated individuals of Dutch origin were overrepresented compared to depressed and anxious persons in population screenings (De Graaf et al., 2005; De Graaf, ten Have, & van Dorsselaer, 2010; De Wit et al., 2008; Peyrot et al., 2013). Furthermore, both the fact that their average self-reported depression score falls in the severe depression category of Beck and colleagues (1996) and the high number of participants with a history of therapy compared to population screenings (Nationaal Kompas Volksgezondheid, 2013) show our sample was more severely depressed than average patients (e.g. Dorrepaal, Van Nieuwenhuizen, Schene, & De Haan, 1998; Schotte, Maes, Cluydts, De Doncker, & Cosyns, 1997; Svanborg & Åsberg, 2001). The third limitation is the small size of our anxiety sample, which limits the generalizability of the outcomes.

Another important matter when interpreting the results is that our research question was based on the assumption that depressed and anxious individuals show WM deficits. Although the majority of studies indeed show that effect (e.g. Basten et al., 2011; Bishop, 2009; Harvey et al., 2004; Joormann & Gotlib, 2008; Whitmer & Banich, 2007), empirical evidence is inconsistent. For instance, Grant, Thase and Sweeney (2001) established depressed outpatients only suffered from small WM deficits. Findings of Barch, Sheline, Csernansky and Snyder (2003) and Fossati, Amar, Raoux, Ergis and Allilaire (1999) found young depressed patients and healthy controls did not differ in WM functioning. Despite the fact that other studies (Beats, Sahakian, & Levy, 1996; Palmer et al., 1996) found that WM deficits are more pronounced in samples that are comparable to ours - older individuals with severe complaints -, our samples' results on the IST were not different than that of healthy samples of other studies (De Lissnyder et al., 2012).

Another inconsistency in the literature is the effectiveness of WM training. Although results seem to be promising in a broad area and even commercial applications are on the market (e.g., CogMed (www.cogmed.com), Cognifit (www.cognifit.com) and Jungle Memory (www.junglememory.com)), there are doubts about the clinical relevance as well as the utility of the cognitive training programs. A recent meta-analysis of Melby-Lervåg and Hulme (2013) concludes that memory training programs appear to result in short-term, specific training effects only and not in generalized effects, as some of these programs pretend to do. The authors argue that the reported positive findings might be caused by the fact that some of those studies only use untreated control groups. Moreover, when such studies are replicated they fail to find evidence for an effect (Jaeggi, Buschkuehl, Jonides, & Shah, 2011; Bergman Nutley et al., 2011). Another explanation of the positive results might be the use of multiple significance tests without correcting for that, which might lead to a large Type I error rate (Melby-Lervåg & Hulme, 2013; Shadish, Cook, & Campbell, 2002). Moreover, the observed moderate effect size in this meta-analysis may actually be lower because of a publication bias (c.f. Cuijpers, Smit, Bohlmeijer, Hollon, & Andersson, 2010; Scherer, Langenberg, & von Elm, 2007). The authors conclude that WM training can result in positive effects on tasks and abilities that are close to those trained but is no suitable treatment for disorders related to WM deficits. This conclusion is in line with a study from Onraedt and Koster (2014), which showed that a WM training in students

with heightened rumination scores did not lead to a reduction of their rumination and depression, neither to an improved WM. However, it is important to note that these findings do not concern training participants suffering from severe psychopathology, like the positive effects of training in schizophrenia and addiction (Houben et al., 2011; Subramaniam et al., 2012).

In sum, in line with positive results of training WM in other psychopathology (e.g. Chein & Morrison, 2010; Houben et al., 2011; Klingberg et al., 2002, 2005; Subramaniam et al., 2012) this study showed training WM led to a significant reduction of anxiety. However, no effects were found on depression and rumination and on WMC. This lack of effect confirms the critical recent findings that WM training does not lead to generalized effects (e.g. Melby-Lervåg & Hulme, 2013). Future experimental research has to show which components may determine a potential effect.

Appendix A

Table 3. Mean (and standard deviations) on the BDI-II, STAI and RRS in the depression sample

	BDI-II		STAI trait		STAI state		STAI total		RRS	
Measurement	WM training	Placebo training	WM training	Placebo training	WM training	Placebo training	WM training	Placebo training	WM training	Placebo training
Pre	33.52 (8.66)	29.61 (9.66)	62.83 (7.91)	59.00 (8.39)	50.12 (9.70)	48.38 (11.51)	112.95 (15.93)	107.38 (18.16)	62.33 (10.73)	62.79 (11.91)
Post	26.83 (10.32)	21.43 (9.64)	59.02 (9.27)	53.98 (10.19)	47.24 (12.38)	44.81 (10.57)	106.26 (19.98)	98.79 (18.45)	57.48 (12.00)	56.00 (12.72)
Follow-up	26.41 (10.70)	21.21 (10.37)	43.38 (3.54)	44.18 (4.16)	47.48 (3.99)	46.93 (5.32)	90.86 (6.42)	91.11 (7.37)	56.17 (12.15)	53.50 (12.48)

Chapter 4|

A Working Memory Training to Decrease Rumination in Depressed and Anxious Individuals

This chapter is in press as: Wanmaker, S., Geraerts, E., & Franken, I.H.A. (submitted). A working memory training to decrease rumination in depressed and anxious individuals: A double-blind randomized controlled trial. *Journal of Affective Disorders.*

Abstract

Rumination is one of the hallmark characteristics of both anxiety disorders and depression, and has been linked with deficient executive functioning, particularly working memory (WM). Previous findings show that working memory capacity can be increased by training. The current study explored by means of a double-blind randomized controlled trial whether an adaptive WM training could increase WMC and by that, reduce rumination, anxiety and depression in a sample of 98 patients with symptoms of anxiety and/or depression. Results show that a WM training did not lead to an overall reduction of rumination, depression, nor anxiety. Neither a positive effect of training was found on WMC. Limitations of this study are the high drop-out rate in both groups (20.11% from pre- to post-training) and the overrepresentation of men and use of anti-depressants in the placebo group. Overall, results show that WM training in patients with symptoms of anxiety and/or depression does not result in reduced rumination nor in reduced symptoms of depression and anxiety. We discuss potential explanations for these findings.

Mood and anxiety disorders are the most prevalent psychopathological disorders (De Graaf, Ten Have, & Van Dorsselaer, 2010). The World Health Organization even predicts that by the year 2020 depression will be the second leading cause of global disability burden (Murray & Lopez, 1997). The prevalence of these disorders has remained stable over decades despite a large number as well as variety of treatments (De Graaf, Ten Have, Van Gool, & Van Dorsselaer, 2012), like pharmacotherapy (Mitte, 2005; Williams et al., 2000) and cognitive-behavioral therapy (CBT; Butler, Chapman, Forman, & Beck, 2006; Cuijpers & Dekker, 2005; Dobson & Dozois, 2001). One of the reasons for this stable prevalence is the high relapse rates in these disorders (Baljon, 2007; Bystritsky, 2006; Bruce et al., 2005). An underlying factor, which therapy and medication are not able to tackle, might explain the persistence of these anxiety and depression symptoms. The cognitive deficits that are found in anxious and depressed individuals might be a candidate for this factor. The aim of the present study was to tackle these cognitive deficits by a new training to increase working memory capacity (WMC).

Working memory functioning in depressed and anxious individuals

Working memory (WM) is a system responsible for these dysfunctioning cognitive processes. This limited-capacity multi-component system is part of our memory system and responsible for active maintenance of information during ongoing processing or distraction of information (Conway et al., 2005). Therefore, working memory capacity (WMC) is 'the extent to which goal-relevant information is kept in an active state in WM, despite the interference of irrelevant information' (Unsworth & Engle, 2007). Furthermore, WM temporary stores, maintains and activates information and is therefore essential to a variety of cognitive functions including reasoning, comprehension and learning. Depression and anxiety symptoms like difficulties in learning (Grossman, Kaufman, Mednitsky, Scharff, & Dennis, 1994; Porter, Gallagher, Thompson, & Young, 2003; Zakzanis, Leach, & Kaplan, 1998), attention (Moritz et al., 2001; Porter et al., 2003; Zakzanis et al., 1998), concentration (Zakzanis et al., 1998), decision-making (Murphy et al., 2001) and planning (Beats, Sahakian, & Levy, 1996; Elliott et al., 1996; Moritz et al., 2001), are a direct expression of these WM deficits since WM controls all these functions.

Anxiety and depression are related to deficits in the three WM key processes; inhibition, updating and shifting (Jonides et al., 2008; Miyake & Shah, 1999; Nee & Jonides, 2008). Firstly, depressed and anxious individuals have difficulties to inhibit irrelevant information from entering their WM (Lemelin et al., 1996; Eysenck, Derakshan, Santos, & Calvo, 2007; MacQueen, Tipper, Young, Joffe, & Levitt, 2000; Monsell, 1996; Trichard, et al., 1995). The second process in which healthy controls and depressed – not anxious – patients differ is updating, which means that depressed patients are less able to remove negative – not positive – information from their WM after it has entered (Joormann & Gotlib, 2008; Levens and Gotlib, 2010; Whitmer & Banich, 2007). These difficulties found in updating might lead to maintenance of negative material in WM (Harvey et al., 2004; Joormann & Gotlib, 2008; Whitmer & Banich, 2007), and thus sustain a negative mood. The third key process is shifting, which refers to the skill to shift attention between different tasks, operations or mental sets (Miyake et al., 2000). Anxious as well as depressive individuals show difficulties shifting from respectively anxious or negative to neutral information (Harvey et al., 2004; MacLeod & Mathews, 1988; Rogers et al., 2004). This shifting difficulty underlines their bias for negative stimuli (Nolen-Hoeksema, 2000) and might lead to a continuation of their anxious image of the world (e.g. Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van Ijzendoorn, 2007). WM deficits might thus play a major role in both the onset and continuation of a negative or anxious mood.

Rumination, a key characteristic in both disorders, is also related to WM deficits. Rumination is the most maladaptive form of self-reflection, which is most strongly related to depression (Mor & Winquist, 2000). This passive way of coping with distress can be defined as repeated uncontrollable negative thoughts about the possible causes and consequences of the experienced distress (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). In this study we define rumination, according to Nolen-Hoeksema and colleagues (2008), as a thinking style rather than that we focus on the specific content of thoughts. Rumination can be divided in two components; reflection and brooding. The first component is one's engagement in cognitive problem solving to decrease negative thoughts, whereas brooding refers to one's passive focus on depressive symptoms and the reasons for their distress.

There are several explanations for the association between rumination and WM deficits. Recent studies clearly show that rumination consumes WM resources (Philippot & Brutoux, 2007), which negatively affects WMC and performance on a (daily) task (Eysenck & Calvo, 1992). For instance, high ruminators had less WMC left when they worried than when they thought about a non-worry topic (Hayes, Hirsch, & Mathews, 2008; Rapee, 1993). In addition, high ruminators had more difficulties with the inhibition for emotional words than low ruminators (Joormann, 2006). Furthermore, Watkins and Brown (2002) showed that a rumination induction led to worse WM functioning in depressed individuals compared to healthy controls, whereas their WMC was similar when they did not ruminate.

The direction of the causal relation between rumination and WMC might also be inverted. That is, WM deficits might cause problems in the inhibition key process, and thus decrease the ability to inhibit negative thoughts resulting in rumination. This cause and effect relation can also explain the sustained negative affect in mood and anxiety disorders (Nolen-Hoeksema, 2000). To further disentangle the role of WM in rumination and sustained negative affect, studies focused on the comparison of individuals with a high and those with a low WMC. As expected, due to their difficulties with the inhibition of negative thoughts, individuals with a low WMC suffered more from intrusions and avoidant thinking (Brewin & Smart, 2005; Klein & Boals, 2001; Rosen & Engle, 1998) in comparison with high WMC individuals. In addition, one's WMC proved to be a good predictor for rumination and depression after 6 months (Zetsche & Joormann, 2011). Furthermore, WMC is positively related to the decrease of intrusions after exposure to a traumatic event (Anderson & Spellman, 1995). An interesting experimental study confirmed the effect of WMC on rumination. Daches and Mor (2013) showed that training individuals to inhibit irrelevant negative information resulted in a borderline significant improved inhibition and a reduction in rumination. The described effects might also be a part of the bidirectional relation between WMC and rumination. That is, rumination might cause WM deficits, which in turn increase the ruminative thinking style. Empirical evidence indeed show that a high level of rumination resulted in fewer attentional resources to divert thoughts away from intrusions (Hayes et al., 2008) as well as from irrelevant negative information (Hertel, 1997; Joormann, 2005; Linville, 1996) and thus, result in a negative mood.

These studies show strong evidence WM deficits and rumination are related. This bidirectional influence might be diminished when improving WMC. Empirical studies in the last decade show it might be possible to increase WMC by training WM. This possibility is worth further exploration in anxious and depressed individuals as deficient WM processes might be a vulnerability factor for anxiety and depression (Onraedt, Koster, Geraerts, De Lissnyder, & De Raedt, 2011) and WM deficits seem to be persistent in depressed and anxious individuals (Joormann, 2004; Joormann & Gotlib, 2007; Paelecke-Habermann, Pohl, & Leplow, 2005).

Training working memory

As numerous studies found that training WM can indeed increase WMC (e.g. Jaeggi, Buschkuehl, Jonides, & Perrig, 2008), a WM training could be an option for treatment in depression and anxiety disorders. Individuals who trained their WM showed improved cognitive functions like attention, nonverbal reasoning abilities and response inhibition improved (Chein & Morrison, 2010; Klingberg, Forssberg, & Westerberg, 2002; Klingberg et al., 2005). This improvement of cognitive functions seems to have the intended positive effect on clinical symptoms, such as in children suffering from ADHD (Klingberg et al., 2005), persons with problematic drinking behavior (Houben, Wiers, & Jansen, 2011), and schizophrenic patients (Subramaniam et al., 2012; Wexler, Anderson, Fulbright, & Gore, 2000).

The exploration whether WM training is also effective in the reduction of anxiety and depression symptoms is very recent. Bomyea and Amir (2011) found that individuals who executed an inhibition training experienced fewer intrusions during a thought suppression task and had greater WMC performance relative to the control group. In addition, Hertel (2004) showed that depressed individuals could learn to use explicit strategies to inhibit or forget negative memories. Furthermore, a pilot cognitive control training was a significant addition to treatment as usual (TAU) – medication, group sessions and environment therapy – to reduce physiological mechanisms underlying depression as well as depression symptoms (Siegle, Ghinassi, & Thase, 2007). However, a recent study from Onraedt and Koster (2014) showed that a WM training in high ruminators had no

effect on their rumination, depression symptoms nor WMC. Future studies have to reveal which conditions of a WM training are essential for positive results.

Shipstead, Redick and Engle (2012) tried to analyze which preconditions must be taken into account when designing or choosing a WM training. Firstly, to validly measure the transfer abilities of a WM training, multiple overlapping measurements that differ from the training tasks have to be used. Secondly, the training condition has to be compared with an active control group with double blind randomization (Shipstead et al., 2012). Thirdly, the effect of a training is the most effective when individuals train for at least 3 weeks or 8 hours (Klingberg, 2010). Lastly, adaptivity of the WM training to the level of the participant is essential (Li et al., 2008; Schmiedek, Lovden, & Lindenberger, 2010). That is, easy tasks lead to even more rumination (Takeuchi, Taki, & Kawashima, 2010) whereas a loaded WM of depressed patients results in better performance (Foulds, 1952).

Current study

The current study tried to integrate these preconditions into a WM training in order to tackle rumination (primary outcome measure) and anxiety and depression symptoms (tertiary outcome measures) by increasing WMC (secondary outcome measure), as WMC and these symptoms are strongly related. Consistent with the preconditions depressed and anxious individuals executed 10 hours of WM training that consisted of two well-documented WM tasks. These tasks required the WM processes – shifting, inhibition and updating – which are decreased in depressed and anxious individuals. The choice for WM tasks with a non-emotional content was based on their good psychometric qualities and because we did not want to confront our participants with negative stimuli every training session.

Another aim of the current study was to explore whether the level of psychopathology was predictive for the efficacy of WM training. This research question was based on numerous studies which show the level of rumination (Joormann & Gotlib, 2008; Lyubomirsky & Nolen-Hoeksema, 1995), anxiety (e.g. Basten et al., 2011; Bishop, 2009), and depression (e.g. Harvey et al., 2004, Joormann & Gotlib, 2008; Whitmer & Banich, 2007) are associated with the level of WM deficits. Because of this strong relation, high

ruminating, anxious, or depressed individuals could profit more from a WM training because they have more deficits to tackle. Nevertheless, these deficits could in turn also diminish the effect of the WM training. We used standardized linear regression analyses to explore whether the level of rumination, anxiety, and depression before the training were more predictive for the extent of change in psychopathology and WM deficits in the experimental group compared to the placebo group. The current study was, to our knowledge, the first to explore the efficacy of training WM on rumination as well as anxiety and depression[5].

Methods

Participants

Participants were recruited by announcements about the possibility to participate in research to depression, anxiety and WM in different media, such as fora and local newspapers. Experimenters screened 189 persons who subscribed for the study with the Structured Clinical Interview for the DSM-IV-TR Axis I Disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 1996) to determine whether they met the criteria for a current depression episode or anxiety disorder. In addition, the exclusion criteria included an age under 18 and above 68 years, a current psychosis and substance dependency. Participants were double-blind (experimenter and patient), based on subject number, allocated to one of the conditions. Figure 1 shows the participant flow during the study. Our sample was characterized by a high comorbidity of anxiety and depression, as most clinical samples (Hirschfeld, 2001). 20.62% of participants had both an anxiety and a depression diagnosis. Furthermore, participants with an anxiety disorder suffered from a moderate depression regarding to the categorization of Beck, Steer, and Brown (1996). Participants with a diagnosis of depression were as anxious, measures with the State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983), as inpatients with a psychiatric disorder (Van der Ploeg, Defares, & Spielberger, 1980).

[5] One measure of this study, the ability to recall specific autobiographical memories, is not described in this article since outcomes were not relevant to answer the research questions described in this article. We measured this ability because it is negatively correlated with depression, anxiety and rumination (Harvey, Bryant, & Dang, 1998; McNally, Lasko, Macklin, & Pitman, 1995; Van Vreeswijk & De Wilde, 2004; Williams et al., 2007) and with problem-solving performance (Evans, Williams, O' Loughlin, & Howells, 1992; Pollock & Williams, 2001), which is a WM function. We measured this ability with the Autobiographical Memory Test (Williams & Broadbent, 1986).

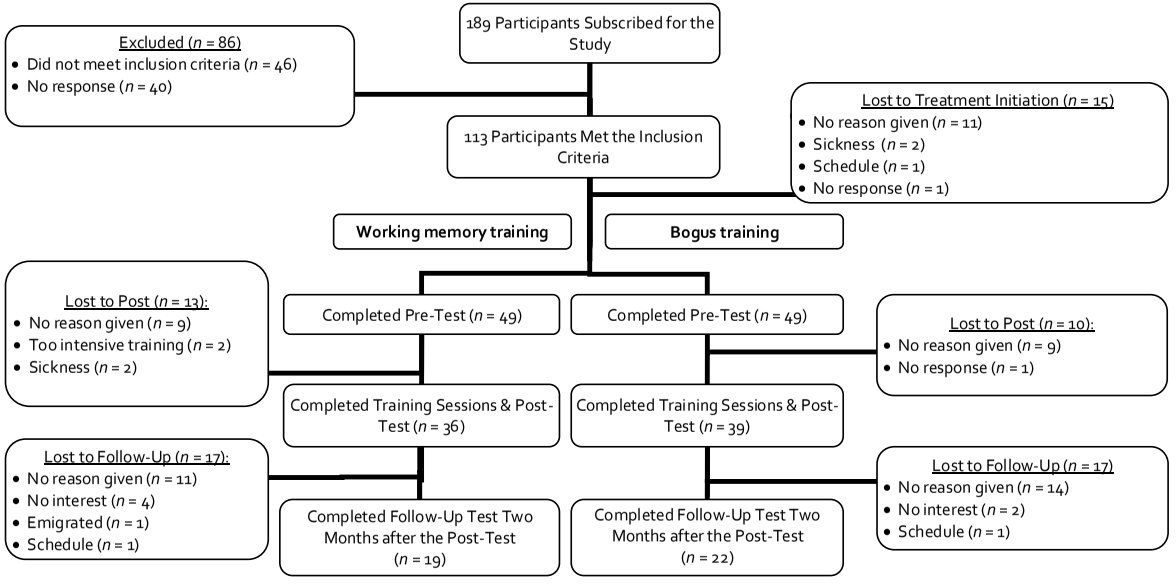

Figure 1. Participant flow

Materials

Diagnosis

The Structured Clinical Interview for DSM-IV Disorders (SCID-I; First et al., 1996, Dutch version; Groenestijn, Akkerhuis, Kupka, Schneider, & Nolen, 1999) is a semi-structured diagnostic interview that covers the axis-I psychopathological disorders. The first author extensively trained the interviewers to administer the SCID-I and supervised them.

Primary outcome measures

Rumination. The Ruminative Response Scale (RRS: Nolen-Hoeksema & Morrow, 1991, Dutch version; Raes, Hermans, & Eelen, 2003; Raes et al., 2009) measures the frequency of self-reported rumination behavior, with answer options ranging from 1 (*never*) to 4 (*always*). The total score of the 22 items (range 22 – 88) was used in the analyses as well as the two subscales with five questions each (both ranges from 5 – 20). The first subscale is reflective pondering, which measures one's engagement in cognitive problem solving. The second subscale, brooding, assesses participants' passive focus on depressive symptoms and the reasons for their distress. The questionnaire shows sufficient reliability (Raes et al., 2009), with a Cronbach's α of .92 in the present study.

Secondary outcome measure

Working memory. WMC was measured by three WM tasks; the Internal Shift Task, Digit Span and Reading Span. These tasks target all WM key processes; shifting, updating, and inhibition. As the two training tasks require the use of these same WM processes, an increase in WMC would be measurable with these three WM transfer tasks.

The Internal Shift Task (IST: De Lissnyder et al., 2012) measures the ability to shift attention between items stored in WM. The task consists of an emotional and a non-emotional condition, the order in which both conditions were presented to the participants was randomized. Pictures of angry and neutral faces of men and women are presented one by one in the middle of the screen. Participants have to count mentally the number of presented men and women in the non-emotional condition and neutral and angry faces in the emotional condition. At the end of the trial they have to report the number of faces in

every category in a fixed order. The trials vary in length from 10 to 14 items, to prevent counting only one category. When participants updated their internal count they have to press the enter key. A new face appears after 200 milliseconds. Every trial consists of shift and no-shift trials, respectively trials where different and similar categories succeed each other. The shift costs per condition (gender and emotional) as well as the average shift costs of the conditions were used in the analyses. Shift costs reflect the effort of shifting attention between the two categories and are measured in reaction time (milliseconds). The IST has good reliability and ecological validity (De Lissnyder, Koster, & De Raedt, 2012).

The second WMC assessment was the Digit Span (Lumley & Calhoun, 1934, script from Woods et al., 2011), which consists of two parts: the forward and backward span, with 14 trials each. The forward Digit Span is a frequently used measure for short term memory, an important subcomponent of the memory system (Shipstead et al., 2012) while the backward version measures WM, especially the updating component. Participants have to recall a series of digits. The forward span starts with 3 and the backward span with 2 digits. The level of the task increases after correct recall of the series whereas an incorrect answer leads to repetition of the level. The level decreases after two adjacent incorrect answers. The level before two adjacent incorrect responses were made was used in the analyses. The psychometric properties of this task are described as good (Kane et al., 2004).

The Reading Span (Daneman & Carpenter, 1980; script from Unsworth, Heitz, Schrock, & Engle, 2005), the third WMC assessment, measures the processing and storage functions of the WM (Shipstead et al., 2012). Participants are required to shift between two tasks: memorize a set of letters and judge the meaning of a sentence as correct or incorrect. The sets range from 3 to 7 letters, each level randomly repeated for 3 times. Participants receive a letter, a sentence and a combination practice phase. The maximal reaction time to judge the sentences in the test phase is their average reaction time in the sentence practice phase plus 500 milliseconds. To make sure participants focus on both parts of the task the goal is to judge 85 percent of the sentences correctly. Beside shifting between the two tasks, participant use the inhibition component of their WM in this task. That is, they have to inhibit the irrelevant information of the first task on the moment they

are focused on the second task. Two variables were used in the analyses. Firstly, the partial-credit unit (PCU) score (Conway et al., 2005), which is the percentage correctly recalled letters. Secondly, the total number of sentence errors, consisting of judging errors and errors due to exceeding the maximal reaction time. The Reading Span correlates highly with the Symmetry Span and Operation Span, which proves WM as underlying construct. Cronbach's alpha varies between .78 en .86 (Kane et al., 2004).

Tertiary outcome measures

Depression. The BDI-II (Beck et al., 1996; Dutch version; Van der Does, 2002) measures the severity of depression symptoms of the last two weeks. This self-report questionnaire contains twenty-one groups of statements about depression symptoms, each with four levels of severity. Adding up the scores of the questions, which range from 0 to 3, results in the total score (range 0 – 63). The reliability of this widely used questionnaire is good (Evers, Van Vliet-Mulder, & Groot, 2005), with a Cronbach's α of .90 in the present study.

Anxiety. The STAI (Spielberger et al., 1983; Dutch version; Van der Ploeg, Defares, & Spielberger, 1979) measures self-reported anxiety, divided in state anxiety and trait anxiety. These subscales respectively measure transient anxiety and dispositional anxiety and both consist of 20 items with a scale ranging from 1 to 4. After pooling some items, both the subscale total scores (range 20 – 80) as the total score of the STAI (range 40 – 160) were used in the analyses. The psychometric qualities of the STAI are good (Bieling, Antony, & Swinson, 1998), with a Cronbach's α of .93 in the state part and .88 in the trait part in this study.

Training

The training paradigm consisted of the Dual N-back task (Jaeggi, Buschkuehl, Etienne, Ozdoba, Perrig, & Nirkko, 2007) and the Symmetry Span (Kane et al., 2004). Participants were instructed to execute the training six times a week and had to start the day after the pre-test. The total duration of the training was approximately 25 minutes a day. Training adherence was 76.67% for the WM training and 71.96 for the placebo training (see Table 1).

The *n*-back task (Kirchner, 1958; Moore & Ross, 1963) is the most extensively used test to measure WMC (For a review, see Kane & Engle, 2002). In the dual *n*-back task, which was used in the present study (script from Jaeggi et al., 2010), participants need to update the information in their WM constantly and are required to shift between two different stimuli. The task consisted of trials consisting of *n* + 20 auditory and visual stimuli in which the participant must continuously indicate whether the item matches the item that appeared *n* items ago in the string. Visual stimuli consisted of a blue square that could appear on 8 different locations whereas the auditory stimuli included 8 consonants. Stimuli appeared for 500 ms and interstimulus interval was 2500 ms. Participants had the entire 3000 ms to press the A key when the visual stimuli matched the *n*-back stimulus and the L key when they observed a match between the letters. *N* ranged from 1 to 5 in the experimental group. To train someone's WM maximally the training adapted to the level of the participant. Three errors or less on both the auditory and the visual part resulted in a higher level whereas five errors or more on one of the two parts led to a lower level. Participants continued on the same *n*-back level between these ranges. The placebo group received the so-called 0-back task, in which participants needed to compare the stimuli with the first seen stimuli. In this way participants did not train their WM since the only cognitive process they used was their short term memory to remember the first-seen stimuli. The pre and post measurements consisted of 10 trials and the training of 13 trials. To check if the training increased experimental group's WMC the maximal achieved n-back level was compared between the measurements. In the control group we compared the average amount of visual and auditory hits and correct rejected items.

The second training task, the Symmetry Span (script from Unsworth et al., 2005) is a typical WM task in which participants have to memorize the order and location of a set of squares while judging the symmetry of images. Firstly, participants had to memorize the location of a red square in a 4 by 4 grid. Participants were required to recall the location of the red squares in correct order at the end of the trial. The red squares were alternated with patterns of white and black squares in an 8 by 8 grid, whose vertical symmetry had to be judged by participants. Half of the images were symmetrical. The experimental group received a WM training that adapted to their performance. If they made an error in one or both parts of the test they continued on the same level, while the level increased when they

made no errors. The experimental group started with a set of 2 squares and received 17 trials in which the maximal set was 12 squares. Contrary, the placebo group's level stayed the same – 2 squares – all 29 trials to prevent training of their WM. Participants could practice each part of the task. Their average response time on the symmetry practice trial plus 500 milliseconds was used as their maximal response time in the test phase. To measure whether the training increased the experimental group's WMC we compared the highest achieved level on the pre- and post-test. The control group's achievement was measured with the percentage correctly recalled squares and the total amount of symmetry errors. The reliability of the Symmetry Span is high (Unsworth, Redick, Heitz, Broadway, & Engle, 2009), with an internal consistency of $\alpha = .86$ (Kane et al., 2004).

Procedure

The study was conducted in line with the Declaration of Helsinki, approved by the Medical Ethical Committee of the Erasmus University Rotterdam, and registered at ClinicalTrials.gov (ID: NCT02119975). Participants executed the pre- and post-measurements in the laboratory of the Erasmus University Rotterdam, the Netherlands. At the pre-test they first signed an informed consent before they began with the questionnaires tapping socio-demographic information, therapy and medication history and the psychopathological self-report questionnaires. Hereafter they executed the IST, Reading Span, Digit Span, Symmetry Span and Dual N-back task. At the end of the pre-test they received a booklet with information about the training and contact information. Furthermore, experimenters instructed participants to evoke the positive feelings (like control) they would experience during the WM training when they had anxious and/or depressive feelings or thoughts or were confronted with difficult situations. The aim of this instruction was twofold. Firstly, the positive experience could help participants to cope with negative feelings and secondly, we tried to activate the association between the training and cognitions. That is, we noticed in other studies it was difficult for participants to relate their negative feelings with the training and this can contribute to drop-out.

Participants had to train six times a week, during four weeks and started the day after the pre-test. They were required to complete the BDI-II, STAI and RRS at the end of every week, thus three times in total. Experimenters monitored participants' training

frequency and completion of the questionnaires and called them when they failed to do that to encourage them to still do it. After four weeks of training, participants executed the post-test. Both measurements consisted of the same measures as the pre-test with exception of the socio-demographic questions. At the post-test participants were asked about their test experience.

Apparatus

The IST was programmed in E-prime 2.0 (Psychology Software Tools, Pittsburgh, PA) and the Reading Span, Digit Span, Symmetry Span and Dual N-back task and the training were programmed in Inquisit 3.0 (2013, Millisecond, Seattle, WA).

Analyses

Data collected on all measures were submitted to mixed design analyses of variance (ANOVA). Each mixed ANOVA included one between-subjects factor for Group: WM training vs. placebo training and Time (pre - post) as within-subject factor. Only relevant analyses to answer the research question are reported, that is; interaction effects (Group x Time) and Time (pre - post) effects[6]. The significance level was set at .05 for all analyses.

Results

Pre-treatment group differences in depression and anxiety samples

As expected exact chi-square tests and two Mann-Whitney tests show the experimental and placebo group do not differ on the majority of socio-demographic variables (see Table 1). However, the placebo group consisted of more men (χ^2 (1) = 5.88, p < .05, OR = .37), and more participants used anti-depressants (χ^2 (1) = 8.83, p < .01, OR = 3.74).

[6] To explore the effects on a longer term we also used mixed ANOVAs including a follow-up measurement, two months after the post-test. Results did not differ from pre-post analyses, psychopathology follow-up scores can be found in Table 3.

Table 1. Socio-demographical characteristics and diagnosis per group

	Working memory training *n* = 49	Placebo training *n* = 49	χ^2 / *t*
% Men	38.8	63.3	χ^2 = 5.88
% Dutch nationality	100	100	N.a.
% High education level	42.9	53.1	χ^2 = 1.02
Age in years	46.63 (12.26)	47.43 (11.71)	*z* = .33
% Use of medication	57.1	59.2	χ^2 =.04
% Use of antidepressants	20.4	49.0	χ^2 = 8.83
% Use of anxiolytics	6.1	6.1	χ^2 = .00
% Currently in therapy	34.7	38.8	χ^2 = .18
% History of therapy	79.6	87.8	χ^2 = 1.10
% History of hospital admission	16.3	12.2	χ^2 = .33
% Sport participation	59.2	71.4	χ^2 = 1.62
Number of training sessions	18.14 (7.67)	17.27 (7.42)	*z* = -.50
% Current depressive episode	31.3	40.8	χ^2 = .96
% History of depression	68.8	59.2	χ^2 = .96
% History of anxiety disorder	70.8	63.3	χ^2 = .63
% Agoraphobia with panic	12.5	16.3	χ^2 = .29
% Agoraphobia without panic	14.6	4.3	χ^2 = 3.18
% Panic disorder	22.9	10.2	χ^2 = 2.85
% Social phobia	22.9	20.4	χ^2 = .09
% Specific phobia	4.2	8.2	χ^2 = .67
% Obsessive-compulsive disorder	10.4	4.1	χ^2 = 1.45
% Post-Traumatic Stress Disorder	2.1	4.1	χ^2 = .32
% Generalized Anxiety Disorder	16.7	24.5	χ^2 = .91
% Hypochondria	6.3	0.0	χ^2 = 3.16
% Anxiety Disorder N.O.S.*	6.3	8.2	χ^2 = .13
% Anxiety disorder and depression diagnosis	14.58	26.53	χ^2 = 2.80

*Note: N.O.S. = Not otherwise specified

Comparing working memory training and placebo training

Training tasks. As the two groups received different interventions, we measured improvement on the trained tasks for both groups separately. The WM training group improved on the highest achieved N-back level significantly from pre- to post-measurement ($z = 4.64$, $p < .01$, $r = .80$; see Table 2). In addition, their level of the Symmetry

Span also increased over time (z = 4.77, p < .01, r = .82; see Table 2). The placebo group improved significantly on the average amount of visual and auditory hits and correct rejected items (z's > 3.57, p's < .001, r's > .58) and the percentage correctly recalled squares (z = 3.26, p < .01, r = .54). Their errors on the symmetry part of the task did not decrease (z = -.95, p > .05, r = -.16).

Table 2. Mean (M) and standard deviations (SD) of the two groups on the working memory training tasks at pre- and post-measurements

	Pre		Post	
	M	*SD*	*M*	*SD*
Highest N-back level (EG)	2.11	.48	3.39	.93
Highest Symmetry Span level (EG)	4.54	1.13	6.53	1.80
Average visual hits (PG)	5.13	9.17	5.75	.97
Average auditory hits (PG)	4.70	1.54	5.73	.99
Average visual correct rejections (PG)	13.75	.31	13.94	.11
Average auditory correct rejections (PG)	13.68	.30	13.94	.12
Percentage recalled squares (PG)	.90	.09	.94	.16
Total symmetry errors (PG)	3.70	4.53	3.67	7.03

Note: EG = Experimental group; PG = Placebo group

Primary outcome measure

Rumination. Unexpectedly, training one's WM did not result in less rumination in comparison with the placebo training, measured with the total scale (F (1, 72) = .04, p > .05, *partial* η^2 = .01). Neither an effect on brooding or reflection was found as a result of training WM (F's (1, 72) < .40, p > .05, *partial* η^2 < .01). Nevertheless, table 3 shows rumination decreased in both groups during the study on both the total and the subscales (F's (1, 72) > 11.00, p < .01, *partial* η^2 > .13).

Table 3. Mean (M) and standard deviations (SD) on the psychopathology measures at pre-, post-and follow-up measurements

	Pre		Post		Follow-up	
	M	*SD*	*M*	*SD*	*M*	*SD*
RRS total	56.61	12.97	50.42	14.28	47.56	14.30
RRS reflective pondering	10.08	3.08	9.01	3.11	8.49	3.18
RRS brooding	11.46	2.88	10.28	3.29	9.68	2.99
STAI total	104.96	18.49	94.14	22.82	86.73	25.17
STAI state	49.03	11.08	44.51	11.95	41.49	12.47
STAI trait	55.93	8.85	49.62	12.08	45.24	13.59
BDI-II	21.46	10.16	14.72	10.83	11.63	11.82

Secondary outcome measures

Working memory.

IST. Against expectations the shifting abilities of the WM training group were not improved as compared to the placebo group; all shift costs; (F (1, 67) < 1.92, p > .05, *partial* η^2 < .03). However, both groups' global shift costs (F (1, 63) = 5.79, p < .05, *partial* η^2 = .08) and emotion shift costs (F (1, 67) = 5.15, p < .05, *partial* η^2 = .07) decreased over time. Shift costs in the gender condition did not change over time (F (1, 67) = 2.19, p > .05, *partial* η^2 = .03).

Digit Span. The results of this WM task are contradictory. The analysis did not show any interaction effects of Group x Time on the forward score (F (1, 69) = 1.42, p > .05, *partial* η^2 = .02). Contrary to expectation the WM training led even to a reduction of the backward score compared to the placebo group (F (1, 68) = 4.85, p < .05, *partial* η^2 = .07; see Table 4). This contradictory effect was reflected in the Time effects. The forward score (F (1, 69) = 51.97, p < .01, *partial* η^2 = .43) of all participants – independent of Group – increased from the pre to the post measurement. In contrast to the forward condition participants' scores significantly decreased on the backward score (F (1, 68) = 24.24, p < .05, *partial* η^2 = .26).

Table 4. Mean (M) and standard deviations (SD) of the two groups on the working memory transfer tasks at pre- and post-measurements

		Working memory training		Placebo training	
		M	*SD*	*M*	*SD*
IST global shift costs	Pre	416	208	323	207
	Post	338	181	293	154
IST emotion shift costs	Pre	452	260	331	226
	Post	353	203	307	180
IST gender shift costs	Pre	382	237	335	202
	Post	348	205	296	182
Digit Span forward score	Pre	4.85	1.02	5.05	1.25
	Post	5.65	1.07	6.16	1.17
Digit Span backward score	Pre	6.24	1.02	5.94	.95
	Post	4.85	1.18	5.42	1.30
Reading span PCU score	Pre	.63	.24	.69	.14
	Post	.69	.17	.66	.21
Sentence errors	Pre	9.79	6.33	8.81	2.85
	Post	7.68	5.70	11.24	8.30

Note: Reading span PCU score = Reading span partial-credit unit score

Reading Span. A Group x Time interaction effect was significant (F (1, 69) = 4.85, $p < .05$, *partial* $\eta^2 = .07$), which implied that the WM training resulted in a better WM than the placebo training (see Table 4). In line with this result was the positive effect of the judging of the sentences (F (1, 69) = 8.75, $p < .05$, *partial* $\eta^2 = .11$). No Time effect was found on any of these two variables (F (1, 69) > .28, $p > .05$, *partial* $\eta^2 = .00$).

Tertiary outcome measures

Anxiety. Against our hypotheses the WM training did not lead to a significant interaction effect of Group x Time on anxiety (all scales: F (1, 72) < .54, $p > .05$, *partial* $\eta^2 < .01$). In line with the reduction of rumination, anxiety reduced over time in both groups (see Table 3) as all STAI scales decreased significantly (F (1, 72) > 12.47, $p < .001$, *partial* $\eta^2 > .15$).

Depression symptoms. We did neither find a significant interaction effect of Group x Time on the BDI-II; (F (1, 72) = .06, $p > .05$, *partial* $\eta^2 = .00$). However, depression reduced significantly over time (F (1, 72) = 51.50, $p < .01$, *partial* $\eta^2 = .42$; see Table 3).

Predicting recovery

We used linear regression analyses to explore whether the level of rumination, anxiety, and depression before the training were more predictive for the extent of change

in psychopathology and WM deficits in the experimental group than in the placebo group. The standardized change scores on the RRS, STAI total, BDI-II, four Digit Span scores, IST emotional shift costs, and Reading Span score were the dependent variables. The standardized values of the RRS total, STAI total, and BDI-II on the pre-test multiplied by the standardized value of the two groups functioned as predictor. By doing this, we could analyze whether the level of psychopathology on the pre-test better predicted the change in psychopathology or WMC in the experimental group than the placebo group. None of these 27 regression analyses were significant. This means that the level of rumination, anxiety, nor depression better predicted the level of change in psychopathology or WMC in the experimental group than in the placebo group (all R^2's < .14, B's < .23, *p's* > .05).

Discussion

The present study explored whether training WM could reduce rumination, and symptoms of depression and anxiety by increasing WMC. The WM training resulted in improved performance on the trained tasks. However, this effect of training did not result in consistent transfer to an increased WMC. That is, the training led to better WM performance on the Reading Span, but in unchanged IST scores and even in worse performance on the Digit Span backward compared to the placebo training. This inconsistent effect on WMC might be the cause of the absent effect of training WM on psychopathology. Participants who executed a WM training did not suffer from less rumination, anxiety or depression compared to the placebo training. However, independent of condition, participants' rumination, anxiety and depression decreased when comparing the pre and post measurements. The level of psychopathological complaints on the pre-test was neither predictive for the effect of WM training on WMC nor on psychopathology.

The lack of effect on WMC and psychopathology is in line with the recent study of Onraedt and Koster (2014). Some meta-analyses and reviews (e.g. Melby-Lervåg & Hulme, 2013; Shipstead et al., 2012) also stress that results of WM training are only present on short-term but that WM training does not lead to generalized effects. Moreover, the publication bias might even lower the found moderate effect size (c.f. Cuijpers, Smit, Bohlmeijer, Hollon, & Andersson, 2010). The cause of the inconsistency of results might be

methodological issues, such as inadequate controls and measurements (Shipstead, Redick, and Engle, 2010). However, both the current study and the study of Onraedt and Koster (2014) have a strong methodology and fail to find an effect of WM on rumination. This might indicate WM training, without any addition of therapy, is not the right intervention for diminishing rumination.

Remarkably, the effects on the transfer tasks were quite inconsistent. The extent of overlap in WM processes required in the training and transfer tasks might explain this inconsistency. That is, the transfer task in which participants' performance increased after training (Reading Span) required exactly the same WM processes as one of the training tasks (Symmetry Span). Moreover, their design had a great overlap. The task on which their performance remained stable measured the same WM processes as the trained tasks, but the designs differed. Lastly, the task on which their performance decreased only overlapped with one WM process required in the training tasks and had a different design. Another reason for the decline in performance of the experimental group on one of the transfer tasks might be that this was the last of the three transfer WM tasks. Participants might have been tired and less concentrated because of the intensive other WM tasks they just finished. Yet another possibility is that the experimental training group was less motivated to execute the post-test compared to the placebo group. They rated the intensity and level of the training as harder than the placebo group, which might have negatively affected their motivation for the WM transfer tasks at the post-measurement.

Another aim of the current study was to explore whether participants' level of psychopathology before the training was predictive for the efficacy of WM training on their WMC and rumination, anxiety, and depression. Against expectation, psychopathology on the pre-test did not predict the reduction of psychopathology or increase of WMC better in the experimental group than in the placebo group. This absent effect could be explained by the lack of effect of WM training. Another possibility for this effect, as well as for the general absence of psychopathological effects, is that depressed and anxious individuals do not differ in WM functioning. If they do not differ in WMC, this intervention might not be the most effective treatment, as it aimed to decrease symptomatology by tackling WM deficits. We based our assumption of deviant WM functioning of these groups on studies

that found differences between depressed and anxious individuals and healthy controls (e.g. Basten et al., 2011; Bishop, 2009; Harvey et al., 2004; Joormann & Gotlib, 2008; Whitmer & Banich, 2007). Nevertheless, other studies show depressed outpatients only suffered from small WM deficits (Barch, Sheline, Csernansky, & Snyder, 2003; Fossati, Amar, Raoux, Ergis, & Allilaire, 1999; Grant, Thase, & Sweeney, 2001; Harvey et al., 2004). The finding that our sample had comparable shift costs as non-depressed students is in line with these results (De Lissnyder et al., 2012). However, our sample scored worse than both healthy and depressed samples on the Digit Span (Harvey et al., 2004). Future research needs to reveal whether WM deficits are specific for a particular sample of depressed and anxious individuals or if they seemed to be general in these disorders.

The results might also be influenced by the characteristics of the sample as it deviates from the average patient sample. One of the causes of this difference might be the recruitment by several media instead of via mental health organizations. One of the deviant characteristics is the average age of our sample (M = 47.03), which is higher than the typical age range in which depression (Nationaal Kompas Volksgezondheid, 2013) and anxiety (Nationaal Kompas Volksgezondheid, 2013; Penninx et al., 2011) is most prevalent. Another deviant characteristic is the high education level of our sample compared to the general Dutch population (Centraal Bureau voor de Statistiek, 2013). Lastly, 91% of our participants have been in therapy and/or are currently in another form of therapy. This is a very high rate compared with the population screenings that indicate that only half of the depressed individuals visit general practitioners (GP; Nationaal Kompas Volksgezondheid, 2013). This proportion is even a smaller in clinical anxious individuals (Nationaal Kompas Volksgezondheid, 2013). Since in the Netherlands GPs refer patients to mental health institutions this emphasizes the high rate of participants in our sample who searched for help for their problems. Thus, it might be that the efficacy of WM training is slightly influenced by the characteristics of our sample.

When we compare our results with that of other studies exploring the effect of cognitive training in depressed or anxious samples it seems that WM training might be effective, but only in combination with TAU. The study of Bomyea and Amir (2011) showed, in contrast to

our results, that it is possible to increase WMC and by that, reduce intrusive cognitions. However, their sample consisted of healthy students. Onraedt and Koster (2014) used a sample of high ruminators, but found no effect on WMC nor on rumination. As rumination and WMC are strongly related, it might be possible that increasing WMC in a sample consisting of high ruminators – like in the current study as well – is not sufficient to decrease rumination. Depressed patients in the study of Siegle et al. (2007) that executed a cognitive control training in addition to their TAU experienced a larger decrease of their depression symptoms compared to group which only received TAU. Although their training was more focused on attentional control compared to our training, both interventions trained WM. These results together might indicate training WM in addition to TAU would be more effective in decreasing depression than exclusively training WM.

Even though WM training had no effect on psychopathology compared to the placebo condition, participants in both conditions experienced a reduction of rumination, anxiety and depression from pre to post measurement. This pattern is in line with findings of other studies, which show that anxiety and depression reduce over time (Kruijshaar et al., 2005; Ramsawh, Raffa, Edelen, Rende, & Keller, 2009; Spijker et al., 2002). In addition, both groups improved on the Digit Span forward and IST global and emotion shift costs, which might be caused by a practice effect. Conversely, participants performed worse on the DS backward on the post-test compared to the pre-test. The higher performance of both groups on the pre-test might be explained by perceived pressure as their higher state anxiety on the pre-test may indicate.

Limitations

Several limitations might have had influence on the results. Firstly, this study had a high drop-out rate compared to other studies exploring WM training (e.g. Klingberg et al., 2002; Olesen, Nagy, Westerberg, & Klingberg, 2003; Prins, Dovis, Ponsioen, Ten Brink, & Van der Oord, 2011; Subramaniam et al., 2012). When we focus on studies that trained depressed or anxious participants the drop-out rates are more like those in the current study (Siegle et al., 2007).

Another limitation was the fact that there were more men in the placebo group and that more participants used anti-depressants, despite random allocation. However, men and women did not differ on any of the variables. Although this result does not exclude the influence of gender on the results totally, it indicates the influence will not be strong. Concerning the use of anti-depressants; the impairment of this medication on memory performance is of low intensity and the clinical relevance is questionable (Gorenstein, Caldeira de Carvalho, Artes, Moreno, & Marcourakis, 2006). Moreover, Harvey and colleagues (2004) compared executive functioning of his, partly medicated sample of depressed individuals with the results of Porter and colleagues (2003) who tested unmedicated depressed patients and identified an equal profile of executive impairments. These findings suggest that medication might not have influenced the results of the current study.

The last major limitation concerns participants' expectations about the training and their immediate perception of their WM task performance. Both can have influenced their mood as well as their WMC performance. That is, a negative mood or low expectations might impair performance and this worse performance might decrease their mood. In a positive way, it can enhance their performance and thus their mood as well. We chose to focus on the assessment of psychopathology and not to include other measures, to prevent drop-out due to time concerns.

Directions for future research

Numerous factors might influence the efficacy of WM training, like training tasks, place of training, training duration, and support during training. For that reason it is difficult to conclude about the efficacy of WM training. The preconditions of Klingberg (2010) and Shipstead for analyzing the efficacy of WM training were taken into account in this study. That is, the use of multiple WM transfer tasks, the use of an active control group with double blind randomization, more than 8 hours training, and adaptivity of the training to participants' WMC. Future research could follow some other preconditions in addition. Firstly, multiple overlapping measurements are needed to validly measure far transfer, like rumination in this study. Secondly, raters have to be blind to condition assignment when they use subjective measures of change.

Furthermore, future studies could analyze the efficacy of WM training in addition to therapy. While the therapy focuses on the cognitions underlying rumination, the training tackles the underlying WM deficits. This combination might also result in less drop-out as therapists could encourage their patients to adhere to the training as well. Lastly, the implementation of game elements might help to reduce drop-out and might increase the efficacy of WM training. This suggestion is based on the study of Prins and colleagues (2011), in which game elements positively affected motivation, compliance and performance during training and resulted in a better WMC in children with ADHD.

Conclusion

In sum, training WM did not lead to an increase of WMC, nor reduction of rumination, anxiety and depression. Furthermore, the level of rumination, anxiety and depression was not predictive for the efficacy of WM training. Future experimental research needs to reveal which components in the design and training determine any potential effect.

Chapter 5|

A Randomized Double-Blind Placebo-Controlled Clinical Trial of the Efficacy of Working Memory Training in Substance Use Patients

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Abstract

Substance Use Disorder (SUD) inpatients show impaired working memory (WM) functioning. Previous findings show that training WM results in an improved working memory capacity (WMC) and a decrease of clinical symptoms in a range of disorders, including alcohol addiction. The aim of the current study is to test the efficacy of a 24 session WM training in addition to treatment as usual (TAU) on craving, WMC, substance use, impulsivity, attention bias and psychopathology using a randomized double-blind placebo-controlled trial. One hundred eighty inpatients diagnosed with a cannabis, cocaine or alcohol use disorder and following treatment as usual were included. Sixty-three participants completed the training and post-test. The efficacy of training was measured on outcomes of craving, WMC, substance use, impulsivity, attention bias and psychopathology. Although the WM training resulted in better scores on the trained tasks in both groups, the placebo training resulted in a better and comparable WMC measured with two non-trained tasks. No effect of WM training could be found on craving, substance use, impulsivity, attention bias and psychopathology. The amount of followed training sessions did not have an influence on the efficacy of training on any of the variables. Working memory training in SUD patients seems not effective in increasing working memory capacity. In addition, and plausibly related to this, craving, substance use, impulsivity, attention bias for substance related cues and psychopathology did not reduce after a working memory training in this population.

Daily-life cognitive functions like planning, attention, memory, initiating appropriate behavior, and inhibiting inappropriate behavior are essential to execute goal-directed actions amid possibilities, challenges, and temptations (Baddeley, 1986; Norman & Shallice, 1986). Substance Use Disorder (SUD) patients show impairments in these cognitive functions compared to non-SUD individuals (Lundqvist, 2005; Ratti, Bo, Giardini, & Soragna, 2002), which may explain their difficulty to suppress impulsive behavior resulting in addiction (Verdejo-García, Lawrence, & Clark, 2008). These cognitive deficits are not only predictive for the onset of addiction (Finn & Hall, 2004; Nigg et al., 2006) but also for the maintenance of substance abuse (Franken, Rosso, & Van Honk, 2003; Goldstein & Volkow, 2002). For instance, these deficits negatively affect treatment effect (McCrady & Smith, 1986), which might explain the high relapse rate of individuals suffering from SUD (Silverman, DeFulio, & Sigurdsson, 2012) One of the impaired cognitive functions is working memory (WM; Ambrose, Bowden, & Whelan, 2001; Bolla, Brown, Eldreth, Tate, & Cadet, 2002; Jovanovski, Erb, & Zakzanis, 2005): a memory component that temporarily stores, activates and maintains information (Baddeley, 1992). One's WM capacity (WMC) is critical for controlling behavior (Goldstein & Volkow, 2002), like attentional control (Kane, Conway, Hambrick, & Engle, 2007; Unsworth & Spillers, 2010) and response inhibition (Bobova, Finn, Rickert, & Lucas, 2009; Kane et al., 2007). The impairment of substance abusers on these WM functions is associated with addiction-related behavior, like impaired decision making (Noël, Bechara, Dan, Hanak, & Verbanck, 2007) and a high rate of delay discounting (Bobova et al., 2009; Shamosh et al., 2008).

Promising recent studies show that training can increase WMC (Chein & Morrison, 2010; Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Morrison & Chein, 2011) and can lead to clinically relevant improvements in various populations suffering from cognitive problems, like individuals with ADHD (Klingberg, Forssberg, & Westerberg, 2002; Klingberg et al., 2005), and schizophrenia (Subramaniam et al., 2012). Bickel, Yi, Landes, Hill, and Baxter (2011) found WM training in outpatients in treatment for stimulant use resulted in reduced rates of discounting of delayed rewards. That is, experimental group participants' preference for delayed, but larger rewards increased. Furthermore, Houben, Wiers, and Jansen (2011) showed WM training in hazardous drinkers decreased alcohol intake and this effect was the strongest in participants with relatively high levels of automatic impulses.

Important to note is that no effect of WM training on WMC was found in the study of Bickel and colleagues (2011) and Houben and colleagues (2011) did not measure an effect of training on WMC.

The present study investigated whether a WM training in addition to treatment as usual (TAU) would positively affect craving (primary outcome measure) and substance use (tertiary outcome measure) in a variety of SUD patients (i.e., alcohol, cannabis and cocaine dependent inpatients). To explore whether training resulted in a larger increase of WMC (secondary outcome measure) in the experimental group, we measured WMC with two WM tasks that were not trained. Furthermore, other factors that are both related to WM and substance abuse, like self-reported impulsivity (see for a review: De Wit, 2009), attention bias (Field & Cox, 2008; Franken, 2003) and symptoms of psychopathology like anxiety and depression (Schuckit, 2006) were assessed to explore whether a WM training positively affects these measures as well. Since the amount of completed training sessions influences the effect of training on WM (Jaeggi et al., 2008), we additionally investigated whether the change in level of craving and WMC was dependent of the number of sessions.

Materials and methods

Participants

Participants were inpatients of two units (one for adults and one for adolescents) of an addiction treatment center (Bouman-Medical Health Care (MHC)) in Rotterdam, the Netherlands. Those patients who met the criteria for a diagnosis of cannabis, cocaine and/or alcohol dependence based on the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition Text Revision (DSM-IV-TR; American Psychiatric Association, 2000), were recruited by the experimenters through presentations and individual approach. The study was carried out from May 2012 to June 2014. Participants who experienced a psychotic episode in the last month, who had severe cognitive problems or who exceeded the age range of 16 to 70 years were excluded. All participants were detoxified and followed the treatment as usual in the clinic, which consisted of individual and group cognitive behavioral therapy (CBT) sessions. Based on a p-value of 0.05, a power of 0.8 and an effect size of 0.5 a group of 102

subjects is large enough to obtain a meaningful result. Because the effect size is uncertain due to inconsistent results in this research area, we included 180 subjects to obtain a meaningful result. Figure 1 (see Appendix A) shows the flow of participants and drop-out reasons during the study. Eleven participants participated in the post-test while they had completed too few training sessions (less than 12) to be included in the analyses. This criterion was based on the amount of training sessions other studies needed to find an effect of WM training on WMC (Dahlin, Nyberg, Bäckman, & Neely, 2008; Jaeggi et al., 2008).

Participants were double-blind randomly allocated to the experimental group and to the placebo group, based on subject number (parallel-group, allocation ratio 1:1). Allocation was executed by the principal investigator, thus experimenters and patients were blind for condition. The average number of training sessions did not differ between the experimental (M = 19.73, Sd = 4.02) and placebo group (M = 19.11, Sd = 3.83; U = 512.50, z = -.71, p = .475, r = -.09). Exact Chi-square tests and a Mann-Whitney test show that the experimental and placebo group did neither differ on socio-demographic variables, nor on their substance dependence diagnoses, determined with the Mini International Neuropsychiatric Interview Plus (Sheehan et al., 1998; Van Vliet, Leroy, & Van Megen, 2000; see Table 1). The groups did not differ on the sum of days they used alcohol and/or drugs the month before the pre-test (U = 3590.00, z = -.94, p = .345, r = -.07), the sum of days they experienced problems with drugs or alcohol (U = 3942.50, z = .24, p = .809, r = .02) and the extent they experienced problems with drugs or alcohol (U = 3485.00, z = -1.27, p = .206, r = -.10), which was measured with the Addiction Severity Index (ASI; Hendriks, Kaplan, Van Limbeek, & Geerlings, 1989; McLellan, Luborsky, Woody, & O'Brien, 1980). These questions concern the sum of days participants used alcohol or drugs the month before the pre-test, the sum of days they experienced problems with alcohol or drugs and the average extent of suffering from alcohol or drugs. Data of adolescents and adults were combined, due to a lack of power. As adolescents are equally represented in the experimental and placebo group, a potential influence of this subgroup would be minimal.

Table 1. Socio-demographic characteristics and substance dependency of the two groups

	Working memory training $N = 95$	Placebo training $N = 86$	χ^2 /*U*
% Men	86.0	75.3	$\chi^2 = 2.87$
% Dutch	97.6	97.4	$\chi^2 = .01$
% High educational level	15.6	15.7	$\chi^2 = .13$
Average age in years (*Sd*)	38.53 (12.58)	36.6 (12.92)	$U = 3752.5$
% Use of anxiolytics	16.7	16.0	$\chi^2 = .01$
% Use of antidepressants	16.7	24.7	$\chi^2 = 1.69$
% Alcohol dependent	84.4	84.6	$\chi^2 = .00$
% Drugs dependent	93.7	89.8	$\chi^2 = .59$

Procedure

The study was conducted in line with the Declaration of Helsinki, approved by the Medical Ethics Committee of the Erasmus University Rotterdam, and registered at ClinicalTrials.gov (ID: NCT02119949). All participants received an information letter and signed an informed consent. Written consent was obtained from caretakers of participants younger than 18. The experimenter started with the M.I.N.I. Plus 5.0.0 (Sheehan et al., 1998; Van Vliet et al., 2000) and the ASI to determine participants' primary addiction and its severity. When participants agreed the M.I.N.I. Plus 5.0.0 was recorded, to potentially check the answers when there were doubts about the diagnosis. Participants filled in the self-report questionnaires regarding psychopathology and craving and carried out the Stroop task, the two WM transfer tasks, and the two training tasks. The training started the day after the pre-test and included 24 sessions of 25 minutes each. Participants trained on weekdays in the clinic. After completing the training they executed the post-test, after which participants could choose between a cinema voucher or a token of 7.50 euros. To prevent any influence of the experimenter on the results of subjective measures, like the ASI and M.I.N.I. Plus 5.0.0, different experimenters assessed the test sessions of a participant.

Materials

Mini International Neuropsychiatric Interview Plus

To verify the SUD diagnosis we used the substance dependence and abuse modules of the Mini International Neuropsychiatric Interview (M.I.N.I. Plus 5.0.0: Sheehan et al., 1998; Van Vliet et al., 2000). This structured interview is based on the DSM-IV (American Psychiatric Association, 2000) symptoms and assesses Axis I psychiatric diagnoses. The questions concern the last 12 months before admittance to the hospital as an inpatient. Psychometric measures of this questionnaire are determined as being good (Lecrubier et al., 1997). The interrater reliability, measured in Cohen's Kappa, in the current study was moderate (.49).

Addiction Severity Index

The Addiction Severity Index (ASI: McLellan et al., 1980: Hendriks et al., 1989) is a semi-structured interview that measures the severity of addiction in 25 questions concerning seven problem areas: medical problems, employment problems, drug use, alcohol use, family and social problems, criminality, and psychiatric problems. We used three of these questions to assess the severity of participants' abuse problems. These questions concern the sum of days participants used alcohol or drugs the month before the pre-test, the sum of days they experienced problems with alcohol or drugs and the average extent of suffering from alcohol or drugs. The last question was measured on a five point scale, ranging from 0 (*totally not*) to 4 (*very much*). The ASI is a reliable and valid measure to measure severity of substance abuse and related problems in substance abusers (e.g. Alterman et al., 2000; Appleby, Dyson, Altman, & Luchins, 1997).

Desires for Alcohol Questionnaire and Desires for Drug Questionnaire

The 13-item Desires for Drug Questionnaire (DDQ: Franken, Hendriks, & van Den Brink, 2002) and the 14-item Desires for Alcohol Questionnaire (DAQ: Clark et al., 1996; Love, James, & Willner, 1998) measure instant craving to respectively drug and alcohol. Answer options consist of a 7-point Likert scale, ranging from '*totally disagree*' to '*totally agree*'. Both questionnaires consist of the subscales: negative reinforcement (the relief of negative states), the desire and intention to use drug/alcohol, and perceived control over drug/alcohol use. To calculate the same subscales for both questionnaires we excluded the

item of the DAQ that was removed in the DDQ (Franken et al., 2002), and analyzed the average score per subscale. Subscales of both questionnaires show good reliability and concurrent validity (Franken et al., 2002; Love et al., 1998), with a Cronbach's α of .86 for the negative reinforcement subscale in the current study, of .86 in the desire and intention subscale and of .77 in the control subscale.

Obsessive Compulsive Drug Use Scale and Obsessive Compulsive Drinking Scale

The Obsessive Compulsive Drug Use Scale (OCDUS: Franken et al., 2002) and Obsessive Compulsive Drinking Scale (OCDS: Anton, Moak, & Latham, 1995; Schippers et al., 1997) measure the subjective interference and distress caused by respectively drug and alcohol related thoughts and compulsive-behavior patterns. In the current study we used two versions of the OCDUS; one for cocaine users (OCDUS-coc) and one for cannabis users (OCDUS-can). The drug questionnaires consist of 13 items and the alcohol questionnaire of 22 items with answers that differ per question. We used the scores of two of the three subscales: 1) thoughts and interference and 2) desire and control in all versions, which consist of the same questions but which are slightly differently formulated. The psychometric measures are good (Anton et al., 1995; Franken et al., 2002; Schippers et al., 1997), with an average Cronbach's α of .88 for the obsession subscale and .80 for the compulsion subscale.

Barratt Impulsivity Scale-11

The 30-item Barratt Impulsivity Scale-11 (BIS-11: Patton & Stanford, 1995) measures impulsivity. In the current study we used the sum of scores, which consist of a 4-point Likert scale ranging from 1 (*rarely/never*) to 4 (*almost always/always*). The BIS-11 shows good construct validity (Patton & Stanford, 1995) and internal consistency, with an average Cronbach's α of .76 in the current study.

Beck Depression Inventory - Second Edition

The Beck Depression Inventory - Second Edition (BDI-II: Beck, Steer, & Brown, 1996; Van der Does, 2002) measures the severity of depression in 21 statements, with four levels of increasing severity each. Participants are instructed to choose the option that was the most applicable to them in the last two weeks. The sum of item scores, which range from 0

to 3, was used in the current study. The reliability of this questionnaire is good (Van Vliet et al., 2000), with an average Cronbach's α of .88 in the current study.

State-Trait Anxiety Inventory

The State-Trait Anxiety Inventory (STAI: Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983; Van der Ploeg, Defares, & Spielberger, 1979) measures self-reported anxiety in 40 questions on a 4-point scale. The questionnaire consists of two parts; state and trait anxiety, respectively transient and dispositional anxiety. The current study used both the total and subscale scores. The psychometric qualities of the STAI are good (Bieling, Antony, & Swinson, 1998), with an average Cronbach's α of .93 in the state part and .92 in the trait part in the current study.

Digit Span

The Digit Span (Lumley & Calhoun, 1934) functioned as a transfer WM task to measure the effect of WM training on WMC. The task consists of two parts: the forward Digit Span is a frequently used measure for short term memory, an important subcomponent of the memory system (Shipstead et al., 2012), and the backward version measures WM. Participants have to recall 14 series of digits in each part. The forward span starts with 3 and the backward span with 2 digits. When the participant correctly recalls the series the level increases with one digit while the level repeats after an incorrect answer and the level decreases with one digit after two adjacent incorrect answers. We used the traditional score, which is the score before two adjacent incorrect responses were made, as well as the maximum score, the highest achieved level independent of incorrect responses, of both task parts in the analyses. The psychometric properties of this task are described as good (Kane et al., 2004).

Reading span task

The Reading Span (Daneman & Carpenter, 1980) functioned as a transfer WM task as well. This task measures the processing and storage functions of WM (Shipstead et al., 2012), specifically participants' ability to shift between two tasks and to cope with proactive interference. These two tasks include the memorization of a series of letters as well as the judgment of a sentence as meaningful or not. The sets range from 3 to 7 letters and

sentences, each level randomly repeats 3 times. To ensure participants focus on both parts they are instructed to judge 85 percent of the sentences correctly and receive feedback about their performance on the letter part. In the current analyses we used the total amount of sentence errors and the partial-credit unit (PCU) score (Conway et al., 2005), which is the percentage correctly recalled letters. The internal reliability is good with a Cronbach's alpha between .78 and .86 (Kane et al., 2004).

Stroop task

The Stroop task measures participants' attention bias for addiction related stimuli. Based on the diagnosis of the M.I.N.I. Plus 5.0.0 (Sheehan et al., 1998; Van Vliet et al., 2000) participants were allocated to the cannabis, cocaine or alcohol version of this task. In case of dependence on more than one substance, they received the Stroop task of related to the self-reported main substance. Participants are required to press the key matching the color of the word on the computer screen as fast as possible. The task consists of four sessions, in each session the eight addiction-related and eight matched neutral words are shown four times. Each session words are shown in another color (blue, yellow, red and green). In the current study we measured the attention bias as the difference in reaction time (milliseconds) between addiction-related and neutral words. Trials with an erroneous response and reaction times below 200 and above 2000 milliseconds were excluded from the analysis. The Stroop task shows adequate validity and reliability (e.g. Cox et al., 2006; Strauss, Allen, Jorgensen, & Cramer, 2005).

Training paradigm

Symmetry Span

The Symmetry Span (Kane et al., 2004) is a typical WM task which measures participants' ability to shift between different tasks and to cope with proactive interference. The task consists of two parts which alternate each other. Firstly, participants have to memorize the order and location of a set of red squares, which appear in a four by four grid. Secondly, participants need to judge whether patterns of white and black squares in an eight by eight grid are vertical symmetrical. Half of those patterns are vertical symmetrical. To prevent participants focus on one part of the task they are instructed to judge minimally

85 percent of the symmetry images correctly and they receive feedback about their performance on the red square part.

To train the experimental group's WM optimally the training adapted to their level. This meant the level increased with one item (red square as well as pattern) when they made no errors while the level remained the same when they made minimally one error on one part of the test. This group received 17 trials, starting with a set of two squares and patterns which could increase to maximally 12 items. To prevent training the placebo group's WM they had to recall only two items on all 29 trials. As the two groups received a different training, their scores on the training tasks cannot be compared. To measure whether the training increased the experimental group's WMC we compared the highest achieved level on all measurements. The control group's achievement was measured with the total amount of symmetry errors and the percentage correctly recalled squares. The reliability of the Symmetry Span is high (Unsworth, Redick, Heitz, Broadway, & Engle, 2009), with an internal consistency of $\alpha = .86$ (Kane et al., 2004).

Dual N-back task

The n-back task (Kirchner, 1958; Moore & Ross, 1963) is one of the most extensively used tests to measure WMC and especially updating (for a review, see Kane & Engle, 2002). In the current study we used the Dual N-back task (Jaeggi et al., 2007), which consists of a series of n + 20 visual and auditory stimuli in which the participant continuously needs to indicate whether the presented item matches the item that appeared n items ago in the series. The auditory stimuli are eight consonants, which they hear in their headphone, whereas the visual stimuli consist of a blue square which can appear on eight positions on the screen. Participants have to press the L and the A for a match between respectively the auditory and visual items.

In the experimental group the level of the task adapted to the WMC of the participant to train their WM optimally. The n could vary from 1 to 5. The level increased with one item when the participant made three errors or less on both the auditory and the visual part whereas five errors or more on one of the two parts led to a lower level. The n-back level remained the same between these ranges. To prevent training of WM in the

control group, they received the so-called 0-back task, in which participants only need to compare the stimuli with the first seen stimuli. The pre, post and follow-up measurements included 10 trials and the training 13 trials. To check if the training increased experimental group's WMC the maximal achieved n-back level was compared between the measurements. In the control group we compared the average amount of visual and auditory hits and correct rejected items.

Apparatus

E-prime (Psychology Software Tools) was used for the Stroop task. Inquisit (Millisecond Software, 2003), was used for all WM tasks. All tasks were assessed on a computer with a Windows XP operating system, with a Google Chrome browser for the WM training and questionnaires.

Results

Data analyses

As the two groups received a different training, their scores on the training tasks cannot be compared. Dependent t-tests or Wilcoxon signed-ranks tests were used to compare both groups separately on the trained tasks between the pre and post measurement. Repeated measures analyses of variance (RM ANOVA) were used to analyze the effect of training on the transfer WM tasks, the ASI, self-report questionnaires and the Stroop task with group as between-subject factor. The significance level was set at .05 for all analyses.

The two groups did not differ on any of the variables on baseline, except the DDQ/DAQ subscale negative reinforcement (U = 2878.50, z = -2.39, p = .017, r = -.18). The control group was inclined to report that substance use would relieve their problems on that moment (*Mdn* = 3.25) than the experimental group (*Mdn* = 2.38).

Working memory

Training tasks. To check whether the training increased WM in the experimental group we compared them on the highest achieved level of the Symmetry Span and the

Dual N-back task. As expected, the training led to a higher level on both tasks (z's > 3.02, p's < .003, r's > .55; see Table 2) after the training compared with the pre-test. The control group's performance on the Symmetry Span did not improve. That is, the amount of symmetry errors and percentage correctly recalled squares (z's < 1.81, p's > .071, r's < .35) were not higher on the post-test than on the pre-test. However, their ability to judge whether the target was a hit or not - both on auditory (z's > 2.62, p's < .009, r's > .56) and visual items (z's > 1.99, p's < .046, r's > .42) - increased (see Table 3).

Table 2. Means and standard deviations of trained working memory tasks in the experimental group

	Pre	Post
Highest SS-level	4.32 (1.23)	5.13 (1.65)
Highest N-level	1.80 (.63)	2.64 (.96)

Note: N-level = Dual N-back level; SS-level = Correctly recalled squares in the Symmetry Span task

Table 3. Means and standard deviations of trained working memory tasks in the placebo group

	Pre	Post
Symmetry errors	4.88 (3.98)	3.29 (4.75)
PCU score SS	.89 (.09)	.89 (.16)
Auditory hits	3.83 (1.60)	5.37 (1.26)
Visual hits	4.50 (1.20)	5.29 (1.45)
Auditory correct rejected items	13.40 (.56)	13.72 (.55)
Visual correct rejected items	13.38 (.82)	13.60 (1.12)

Note: SS = Symmetry Span

Transfer tasks

Digit Span. As mentioned before, performance on the WM transfer task (i.e., a non-trained task) is the main index of the efficacy of the WM training. Unexpectedly, no interaction effects on any of the Digit Span variables were found ($F(1,54)$ < 2.17, p's > .146, *partial* η^2's < .01). Both groups, however, performed better on the post-test than on the pre-test on the

Digit Span, seen on the forward traditional, backward span traditional and backward span maximal scores ($F(1,54) > .812$, p's < .024, *partial* η^2's > .09; see Table 4). Their forward maximal score did not improve over time ($F(1,54) = .81$, $p = .371$, *partial* η^2's = .02).

Reading span task. Against our hypothesis the experimental group's performance, measured with the percentage correctly recalled letters, decreased while that of the control group improved ($F(1,52) = 7.89$, $p = .007$, *partial* $\eta^2 = .13$; see Table 4). No interaction effect was found on the total amount of sentence errors ($F(1,52) = .35$, $p = .556$, *partial* $\eta^2 = .01$). Both groups did not become better over time in recalling letters ($F(1,52) = .31$ $p = .580$, *partial* $\eta^2 = .01$) nor judging whether sentences were meaningful or not ($F(1,52) = .018$, $p = .894$, *partial* $\eta^2 = .00$)

Table 4. Means and standard deviations of transfer working memory tasks

	Experimental group		Placebo group	
	Pre	Post	Pre	Post
DS FW Trad	5.42 (1.03)	5.90 (1.47)	5.68 (1.14)	6.00 (1.29)
DS BW Trad	4.35 (1.40)	4.74 (1.59)	5.08 (1.35)	5.72 (1.77)
DS FW Max	6.06 (1.12)	6.19 (1.40)	6.56 (1.00)	6.72 (1.37)
DS BW Max	5.23 (1.71)	5.39 (1.76)	5.72 (1.31)	6.32 (1.44)
PCU score RS	.59 (.22)	.52 (.24)	.62 (.16)	.71 (.18)
RS sentence errors	14.93 (9.53)	15.31 (11.14)	10.72 (6.27)	10.12 (4.68)

Note: DS = Digit Span; FW = Forward; BW = Backward; Trad = Traditional score; Max = Maximal score; RS = Reading Span

Craving

DDQ/DAQ. The expected positive effect of a WM training compared to a placebo training on instant craving was not found. No interaction effect was found on any of the DDQ/DAQ scales ($F(1,58) < 1.46$, p's > .231, *partial* η^2's < .03), neither Time effects ($F(1,58) < 3.89$, p's > .053, *partial* η^2's < .06).

OCDUS/OCDS. Participants who executed the WM training did not experience a larger decrease of thoughts and interference ($F(1,69) = .06$, $p = .804$, *partial* $\eta^2 = .00$) or desire

($F(1,59) = .33$, $p = .568$, *partial* $\eta^2 = .01$) regarding substances than participants in the placebo group. Nevertheless, both groups had less interfering thoughts ($F(1,69) = 20.67$, $p = .001$, *partial* $\eta^2 = .23$) and compulsive behavior ($F(1,59) = 10.33$, $p = .002$, *partial* $\eta^2 = .15$) comparing the pre ($M = 12.35$, $Sd = 4.70$; $M = 5.77$, $Sd = 2.84$) and post ($M = 10.55$, $Sd = 3.66$; $M = 4.64$, $Sd = 1.69$) measurement.

Substance use

ASI. Against our expectations no interaction effect of Group x Time was found on any of the ASI variables. That is, the sum of days they used alcohol or drugs the last 30 days ($F(1,58) = 2.34$, $p = .132$, *partial* $\eta^2 = .04$), the sum of days they experienced problems with alcohol or drugs ($F(1,56) = .14$, $p = .705$, *partial* $\eta^2 = .00$) and the average extent of suffering from alcohol or drugs ($F(1,58) = .34$, $p = .562$, *partial* $\eta^2 = .01$). However, an overall decrease was observed over time. That is, the average sum of days they used alcohol or drugs the last 30 days ($F(1,58) = 108.76$, $p = .001$, *partial* $\eta^2 = .65$) diminished from 43.18 ($Sd = 25.51$) on the pre-test to 4.55 ($Sd = 15.20$) on the post-test. Furthermore, the average sum of days they experienced problems with alcohol or drugs ($F(1,56) = 28.55$, $p = .001$, *partial* $\eta^2 = .34$) decreased from 23.59 ($Sd = 19.16$) to 8.36 ($Sd = 13.00$). Lastly, the average extent of suffering from alcohol or drugs ($F(1,58) = 53.19$, $p = .001$, *partial* $\eta^2 = .48$) declined from 1.51 ($Sd = .91$) to .62 ($Sd = .64$).

Impulsivity

BIS-11. The kind of training did not have an effect over time on participant's impulsivity level ($F(1,58) = .57$, $p = .452$, *partial* $\eta^2 = .01$). A significant time effect ($F(1,58) = 8.00$, $p = .006$, *partial* $\eta^2 = .121$) shows that participants, independent of group, became less impulsive from the pre ($M = 70.35$, $Sd = 8.62$) to the post ($M = 68.12$, $Sd = 9.03$) measurement.

Attention bias

Stroop task. The experimental WM training did not lead to a significant stronger reduction of attention bias for substance related words than the placebo group ($F(1,49) = .267$, $p = .608$, *partial* $\eta^2 = .01$). Neither did participants' attention bias change over time ($F(1,49) = 3.897$, $p = .054$, *partial* $\eta^2 = .07$).

Psychopathology

BDI-II. The experimental group's depressive feelings did not decrease more due to the WM training than those feelings of the placebo group ($F(1,58) = .32$, $p = .572$, *partial* $\eta^2 = .01$). Both groups, however, experienced a reduction of depressive feelings from the pre ($M = 18.33$, $Sd = 11.52$) to post measurement ($M = 12.60$, $Sd = 11.75$; $F(1,58) = 16.47$, $p = .001$, *partial* $\eta^2 = .22$).

STAI. The same trends shown in their depressive feelings were found in their feelings of anxiety. That is, no interaction effects were found on the STAI total and the state and trait subscales ($F(1,58) < .09$, p's $> .760$, *partial* η^2's $< .00$) but a significant effect of Time was found on the STAI total and STAI trait subscale ($F(1,54) > 6.49$, p's $< .014$, *partial* η^2's $> .15$). Participants, independent of group, were more anxious on the pre-test ($M = 88.80$, $Sd = 24.85$; $M = 46.85$, $Sd = 13.00$) than on the post-test ($M = 82.37$, $Sd = 25.11$; $M = 42.82$, $Sd = 13.57$). Contrary, their state anxiety did not diminish over Time $F(1,58) = 2.85$, $p = .097$, *partial* $\eta^2 = .05$).

Regression

To explore whether the amount of completed training sessions was related to the change in level of craving and WMC, we used linear regression analyses using standardized values comparing the WM and placebo training. The difference scores (pre minus post) of the OCDUS/OCDS and DDQ/DAQ subscales and all variables of the two transfer WM tasks were the dependent variables and the number of completed training sessions was the predictor. Unexpected, a higher number of training sessions was not more predictive for a reduction in craving (R^2's $< .14$, B's $< -.12$, *p's* $> .391$) or increase of WMC in the experimental group than in the placebo group (all R^2's $< .14$, B's $< .04$, *p's* $> .282$).

Discussion

This randomized double-blind placebo-controlled clinical trial showed that WMC of SUD inpatients did not increase after WM training. None of the measured substance abuse related measures, like substance use, craving, attention bias, impulsivity and

psychopathology reduced either as a result of training WM. Furthermore, the number of training sessions was not predictive for changes in any measures. The most straightforward explanation for the absent effects of training WM is the lack of effect on WMC, which was hypothesized to be related to addiction related behavior. Although the placebo training remained on a very easy and nonadaptive level in contrast to the experimental training, the placebo group's WMC improved while that of the experimental group decreased. An explanation of this finding might be that their WMC was trained to a larger extent than that of the experimental group. Reasons for that suggestion are experimenters' observation that a significant part of participants in the experimental group experienced the training as very difficult to learn and secondly, the placebo group's score on one of the trained tasks improved. Another factor that differed between the groups was that the control group was more convinced substance use would relieve their problems on that moment than the experimental group. As this result indicates the placebo group was more focused on substance use, it is unlikely that this group difference is the cause of the absent effects of WM training.

Our findings are in contrast with the study of Houben and colleagues (2011), who showed problem drinkers had reduced alcohol intake for more than 1 month after a 25 session WM training. These contrasting results might be explained by differences in participant samples. While Houben and colleagues (2011) used participants who were hazardous drinkers based on the Alcohol Use Disorders Identification Test (AUDIT; Saunders, Aasland, Babor, de la Fuente, Juan, & Grant, 1993), our sample consisted of inpatients who were substance dependent. Furthermore, their sample was recruited by internet advertisements, which might have positively influenced sample characteristics, like motivation, educational level and internet access. Important to note is that Houben and colleagues (2011) did not use any transfer WM tasks. In other words, they only measured change in WMC with trained tasks. In the current study we also found increased scores on trained WM tasks, but not on transfer WM tasks. Thus, it is not certain that an increased WMC was the factor that led to change in alcohol consumption in their study.

The absent effect of WM training on WMC is in line with the study of Bickel and colleagues (2011). They found WM training did not result in increased WMC but that it did

result in reduced delay discounting. The results of Houben and colleagues (2011) and Bickel and colleagues (2011) fit in the criticism of meta-analyses concerning WM training effects. They conclude results regarding generalization of WM training to other skills are mixed and question whether observed generalization is a result of change in WMC (Melby-Lervåg & Hulme, 2013; Shipstead, Redick, & Engle, 2012).

The improvement of participants' substance use, substance related thoughts, desire and control, impulsivity, and psychopathology over time may be attributed to the psychological treatment participants received in the clinic. Remarkably, participants' instant craving, attentional bias, and state anxiety did not reduce over time. Their stable instant craving and attentional bias might be explained by the fact that patients were detoxified and few substance related stimuli were present in the clinic. Such stimuli are required to experience craving (Franken & Van den Brink, 2009; Franken, 2003) and influence the interference of substance related cues in the Stroop task (Cox, Fadardi, & Pothos, 2006). Therefore, the low self-reported craving and Stroop task effect could be a floor effect, which is difficult to change by an intervention. The stable state anxiety might be explained by participants' feelings of anxiety for the WM tasks. A high percentage of participants had a low educational level and some had difficulties with executing the tasks, these factors are related to test anxiety (Hembree, 1988). This result refers to a limitation of this study. The current sample of inpatients had less craving and confrontation with substances than a sample of outpatients generally has, which impairs measurement of those variables. An advantage of our sample was that we could control training compliance, which will be less when outpatients execute a WM training at home. Nevertheless, the current drop-out rate of 65% from pre to post measurement was still very high. The major cause for drop-out was a lack of motivation. A method to prevent drop-out might be spacing of reward instead of one reward at the end of the post-test. For instance, Van Gageldonk, Rigter, Ketelaars, and Van Laar (2005) conclude in their review rewarding desired behavior is one of the most effective methods to motivate substance abusers. A second limitation is experimenters' observation that participants were bored because of executing the same tasks every day and had difficulties to transfer their feelings during the training – like feeling in control – into daily life and when confronted with substance cues or craving. Shipstead and colleagues (2012) mention it is critical for a successful training

program that participants are constantly engaged in the task at a level that is neither boring nor too challenging. In addition, a study of Prins, Dovis, Ponsioen, ten Brink, and van der Oord (2011) showed game elements positively influence motivation and performance during training and resulted in a better WM in children with ADHD. A gamified WM training with direct references to substance cues could be used in future research. The last major limitation of this study is the observation that patients talked to each other about the training, which might have influenced their perception of the group they were in. However, the groups did not differ in their estimation regarding the group they were allocated to.

In sum, the current study did not find an effect of WM training on substance use, craving, attention bias, impulsivity and psychopathology compared to a placebo training. Unexpectedly, the easy placebo training, which did not adapt to WMC, resulted in an increased WMC compared to the adaptive experimental training. Future research needs to explore further whether WMC is the factor that influences substance abuse related behavior.

Appendix A

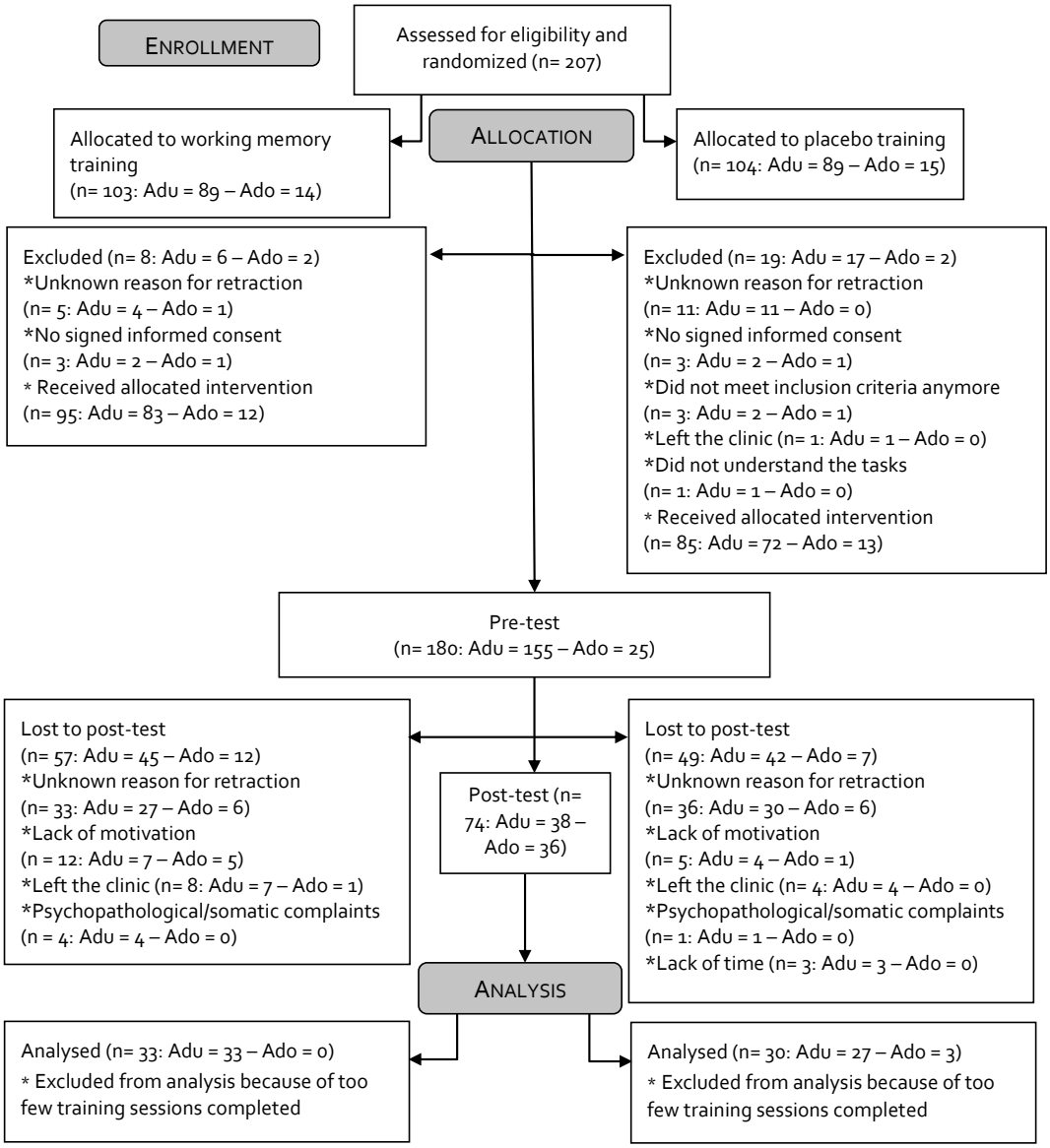

Figure 1. Participant flow

Note: Adu = Adult; Ado = Adolescent

Chapter 6|

Training Students' Working Memory to Improve Academic Performance and Psychological Well-being

This chapter has been submitted for publication as: Wanmaker, S., Geraerts, E., & Franken, I.H.A. (submitted). Training students' working memory to improve academic performance and psychological well-being.

Abstract

An efficient working memory is crucial to a wide range of cognitive functions that are necessary in academic life and for psychological well-being. Previous studies showed that training working memory can increase working memory capacity and might even result in a reduction of psychopathological symptoms. Using an experimental design, the current study examined whether increasing working memory capacity results in an improved academic performance and psychological well-being in first year psychology students. Psychological well-being and other outcome variables were assessed by measuring attentional control, impulsivity, self-control, coping abilities and emotional measures (i.e., levels of anxiety, depression, rumination, intrusions, and stress). In the experimental group, sixty-three students executed a working memory training consisting of two components, which adapted to their working memory capacity. The control group, consisting of 65 students, underwent a similar training but this was conducted on such an easy and non-adaptive level that working memory improvements could not be expected. Results show that training participants' working memory did not result in an improved working memory capacity. In addition, we did not find any improvements on academic performance indices nor psychological well-being. Potential reasons for the lack of effects of training working memory are discussed.

An efficient working memory (WM) is crucial for a wide range of cognitive functions that are necessary in educational life, including learning, planning, comprehension, reasoning, and allocation of attention (Baddeley, 1992). Several conditions are related to impairments in the function of WM, such as stress (Klein & Barnes, 1994) and psychopathology (e.g. Joormann & Gotlib, 2008; Whitmer & Banich, 2007). For instance, high-anxious individuals suffer from WM deficits in stressful situations or under cognitive load (Calvo & Ramos, 1989; Darke, 1988; Eysenck & Derakshan, 1998; MacLeod & Donnellan, 1993; Sorg & Whitney, 1992). In addition, depressed patients show more deficits in inhibiting and removing irrelevant negative information from their WM compared to healthy controls (Harvey et al., 2004; Joormann and Gotlib, 2008; Verwoerd, Wessel, & de Jong, 2009). Furthermore, dysphoric rumination in students leads to impaired attentional control and educational performance (Lyubomirsky, Kasri, & Zehm, 2003). Thus, WM deficits have potential negative effects on educational performance and psychological well-being.

A recent line of research shows that improving WM by training seems to be possible and this can even lead to improvement of abilities necessary for academic functioning, like attention (Chein & Morrison, 2010; Klingberg et al., 2005), nonverbal reasoning (Klingberg et al., 2002, 2005), memory for instructions (Klingberg et al., 2005; Holmes, Gathercole, & Dunning, 2009), reading abilities (Dahlin, 2011; Loosli, Buschkuehl, Perrig, & Jaeggi, 2012) and academic abilities in general (Holmes et al., 2009; Thorell, Lindqvist, Nutley, Bohlin, & Klingberg, 2009). These effects remained significant at 3-month (e.g. Klingberg et al, 2005) and 6-month (e.g. Borella, Carretti, Riboldi, & De Beni, 2010, Holmes et al., 2009) follow-up measurements. As a result of these promising effects of training WM, a new line of research focuses on WM training as a treatment for psychopathology. This idea is based on the findings that individuals suffering from psychopathology have a reduced working memory capacity (WMC), which might be related to their symptoms (e.g. Eysenck, Derakshan, Santos, & Calvo, 2007; Joormann & Gotlib, 2008; Joormann, Nee, Berman, Jonides, & Gotlib, 2010; Westerberg, Hirvikoski, Forssberg, & Klingberg, 2004). Although in some review studies these results have been considered very promising (Klingberg, 2010; Morrison & Chein, 2011), some recent papers critically evaluate these training results (Melby-Lervåg & Hulme, 2013; Shipstead, Redick, & Engle, 2012). Their major criticism

concerns the mixed results of WM training generalization to other skills and whether the observed generalization is a result of changes in WMC (Melby-Lervåg & Hulme, 2013; Shipstead, Redick, & Engle, 2012). Thus, training WM might result in better cognitive functioning leading to improved academic as well as emotional functioning, but these is also some recent criticism and more research is clearly needed.

To our knowledge no study explored the possibility to train healthy students' WM, with the aim to increase their cognitive functioning and by doing so, improve their academic results and decrease potential psychopathological symptoms. The current study attempted to train first year psychology students' WM and monitored the effect on their academic performance, attentional control, coping abilities and emotional measures like anxiety, depression, rumination, intrusions and stress. Moreover, we also measured impulsivity as well as self-control, as WMC seems to be strongly related to these behavioral components (Barret, Tugade, & Engle, 2004; Engle, 2002) and training WM was able to enforce them in a clinical population (Houben et al., 2011). To measure whether the training led to an improved WM, participants executed WM tasks before and after the training. A WM training with two components was used, to see whether these differed in effect. Thus, we hypothesized training WM would lead to an increased WMC, resulting in better academic performance, attentional control, coping abilities and less psychopathological symptoms, stress, and impulsivity.

Method

Participants

Hundred twenty-eight first year Bachelor students (age: M = 19.27, SD = 1.83) of the Erasmus University Rotterdam were recruited from the psychology research website and campus advertisements and flyers. The only inclusion criterion was access to a Windows computer, as this was necessary to perform the training program. Participants with an even student registration number were allocated to the experimental group (n = 63, 7 men) and those with an odd student number to the control group (n = 65, 11 men). All participants were blind for condition. Mann-Whitney tests showed that the average number of training sessions did not differ between the experimental (first WM training component consisting of 5 training sessions: M = 4.70, SD = .85, second WM training component consisting of 6

training sessions: $M = 4.55$, $SD = 2.29$) and control group (first training: $M = 4.41$, $SD = 1.59$, second training: $M = 4.53$, $SD = 2.36$; both training components: $U < 2007.00$, $z < .08$, $p > .05$, $r < .01$). They received course credits for their participation. Mann-Whitney tests showed participants characteristics like age ($U = 1719.50$, $z = -.44$, $p > .05$, $r = -.04$) and gender ($\chi^2(1) = .89$, $p > .05$, OR = 1.63) did not differ between groups. However, there was a marginal significant effect of using aids during the tests or training ($\chi^2(1) = 4.12$, $p = .05$, OR = .30). 21.2% of the experimental group and 7.4% of the placebo group confessed they used aids during the experiment although it was clearly stated it was prohibited.

Questionnaires

Visual Analogue Scale (VAS)

To measure their emotional state participants rated their mood states (sad, anxious, cheerful, relaxed, and angry) on a VAS from 0 to 100, representing percentages.

Beck Depression Inventory-II

The Beck Depression Inventory-II (BDI-II: Beck, Steer, & Brown, 1996; Van der Does, 2002) measures the severity of depression symptoms. This self-report questionnaire consists of 21 groups of statements about depression. Scores range from 0 to 3, which sum up to the total score that indicates the severity of the depression. Participants need to choose the most applicable answer option to them in the last two weeks. The psychometric values of this extensively used questionnaire are good (Evers, Van Vliet-Mulder, & Groot, 2005), with an average Cronbach's α of .89 in the present study.

State-Trait Anxiety Inventory

The State-Trait Anxiety Inventory (STAI: Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983; Van der Ploeg, Defares, & Spielberger, 1979)
measures state and trait anxiety, which are respectively transient and dispositional anxiety. Both subscales consist of 20 items with a scale ranging from 1 to 4, from which half of the items has to be pooled before summing up to the total scores. Both the subscale total scores as the total score of the STAI are used in the analyses. The questionnaire's psychometric qualities are good (Bieling, Antony, & Swinson, 1998), with a Cronbach's α of .93 for both the STAI trait and the STAI state in the present study.

Ruminative Response Scale

The 22-item Ruminative Response Scale (RRS: Nolen-Hoeksema & Morrow, 1991; Raes, Hermans, & Eelen, 2003) measures the frequency of self-reported rumination behavior. The answer options range from 1 (*never*) to 4 (*always*) and sum op to the total score, which is used in the analyses. The questionnaire shows sufficient reliability (Raes et al., 2003), with an average Cronbach's α of .93 in the present study.

Brief Self-Control Scale

The Brief Self-Control Scale (BSCS: Tangney, Baumeister, & Boone, 2004; Kuijer, De Ridder, Ouwehand, Houx, & Van den Bos, 2008) is a self-report questionnaire that measures self-control as a personality trait and consists of 13 items that are applicable to one's self-image. The scale ranges from 1: *not at all like me* to 5: *very much like me* and sums up to the total score, which is used in the current study. The psychometric measures of the questionnaire are favorable (Tangney et al., 2004), with an average Cronbach's α of .85 in the present study.

Barratt Impulsivity Scale-11

The Barratt Impulsivity Scale-11 (BIS-11: Patton & Stanford, 1995) measures impulsivity and consists of 30 statements with a 4-point Likert scale ranging from 1 (*rarely/never*) to 4 (*almost always/always*). After pooling a number of items the total score reflects the extent of impulsivity. The BIS-11 shows good intern consistency (.79-.83, .94 on average in the present study) and construct validity (Patton & Stanford, 1995).

Impact of Event Scale

The 15-item Impact of Event Scale (IES: Horowitz, Wilner, & Alvarez, 1979; Brom & Kleber, 1985) measures intrusion and avoidance symptoms of PTSD experienced over the past week. The 4-point scale ranges from *not at all* to *often* and sum up to the total score. The psychometric quality of the test is good (Horowitz et al., 1979; Van der Ploeg, Mooren, Kleber, Van der Velden, & Brom, 2004), with an average Cronbach's α of .94 in the present study.

Perceived Stress Questionnaire

The Perceived Stress Questionnaire (PSQ: Levenstein et al., 1993) is a measure for stress and consists of 30 items with a scale ranging from 1: *almost never* to 4: *usually*. Participants rate the statements on this scale for the last month. After pooling a number of items the total score is used for the analyses. The psychometric values of this questionnaire are good (Levenstein et al., 1993) with an average Cronbach's α of .95 in the present study.

Attentional Control Scale

The Attentional Control Scale (ACS: Derryberry & Reed, 2002) is a 20-item questionnaire which assesses concentration on a 5-point scale (1: *almost never* to 5: *always*). Higher scores reflect less attentional control. The psychometric values are not available, but a study of Derryberry and Reed (2002) showed that the level of attentional control was an important mediating factor between anxiety and attentional bias. In the present study we found an average Cronbach's α of .86.

Marlowe Crowne Social Desirability Scale

The Marlowe Crowne Social Desirability Scale (MC SDS: Crowne & Marlowe, 1960) measures social desirability and conformity behavior. This self-report questionnaire consists of 32 questions, concerning everyday behaviors, with two answer options; true (1 point) and not true (0 points). After pooling 15 items the total score represents the extent of social desirability. The psychometric values of this test are reasonable (Beretvas, Meyers and Leite, 2002), with an average Cronbach's α of .76 in the present study.

Taylor Manifest Anxiety Scale

This Bendig version of the Taylor Manifest Anxiety Scale (TMAS: Taylor, 1953) assesses anxiety. It comprises 20 questions, derived from the Minnesota Multiphasic Personality Inventory (MMPI). The answer options are true and not true, respectively scored as one and zero. A high score indicates a high level of anxiety. The average Cronbach's α was .87 in the present study.

Utrechtse Coping List

The 47-item Utrechtse Coping List (UCL: Schreurs, Van de Willige, Tellegen, & Brosschot, 1993) measures 7 different coping styles, which are; tackling problems actively, palliative reaction, avoidance, expressive support-seeking coping, passive coping, expression of emotions/anger, and comforting cognitions. We use all subscales in the current study. Answer options consist of a 4-point Likert scale. The psychometric properties of the UCL are generally favorable (Sanderman & Ormel, 1992). The average Cronbach's α in this study was .85 for the UCL in total, .84 for tackling problems actively, .73 for palliative reaction, .62 for avoidance, .82 for expressive support-seeking coping, .74 for passive coping, .66 for expression of emotions/anger and .80 for comforting cognitions.

Study results

To explore whether the training resulted in better academic performance in the WM training group we compared the difference in their marks between the courses before the training components (course 2 and7) and the exam right after the training components (courses 3 and 8) with that of the placebo group. The exams are marked on a 1 to 10 scale, where a score of 10 represents an optimal result.

Transfer Working Memory Tasks

Digit Span Task

While the forward Digit Span Task (DST: Lumley & Calhoun, 1934) is a frequently used measure for short-term memory (Shipstead et al., 2012), the backward version measures WM. Each version consisted of 14 trials of a random string of digits (1 – 9), each digit shown for 1 second, which the participant had to recall by typing the numbers in a response box. Before and after the string a red circle was shown to signal the digit sequence was about to start or that the response box was about to appear. The forward span started with 3 and the backward span with 2 digits. A practice phase of 1 trial preceded the test phase in both versions and matched the start level. In this phase feedback (correct/incorrect) was given to the participant. The level of the task increased after correct recall of the series whereas an incorrect answer led to repetition of the level. The level decreased after two consecutive incorrect answers. For both conditions we analyzed the traditional score, which was the score before two consecutive incorrect responses were

made, as well as the maximum score, the highest level independent of incorrect responses. The psychometric properties of this task are good (Kane, et al., 2004).

Operation Span Task

The Operation Span Task (OST: Unsworth et al., 2005) is one of the most frequently used WM tasks (Conway et al., 2005) and measures updating as well as shifting WM abilities. Participants saw a letter (F, H, J, K, L, N, P, Q, R, S, T, and Y) for 1 second, alternated with a math problem (e.g. (1*2) + 1 = ?) which they had to solve as quickly as possible. Half of these math solutions were false. After the math problem they saw an answer and had to judge whether this answer was true or false by clicking on these words on the screen. At the end of trial they had to recall the letters by selecting them in the right order in a 4 x 3 matrix containing all possible letters. Participants received feedback after the response. Participants practiced the letters (2 times 2 and 2 times 3 letters), math (15 math problems) and the combination of both phases (3 times 2 letters and math problems). In the experimental phase participants received randomly all 5 levels (3, 4, 5, 6, and 7 letters) 3 times each. The maximal reaction time to solve the math problems in the test phase was 2.5 times their reaction time in the math practice phase. To assure participants focused on both parts of the task we told them that we could only use data from participants that judged minimally 85 percent of the math problems correctly. The partial-credit unit (PCU) scoring was used in the analyses (Conway et al., 2005); the percentage correctly recalled items. Further, we analyzed the total number of math errors, these consisted of accuracy errors and errors due to an excessive reaction time. The test showed good internal consistency (α = .78) and test–retest reliability (.83; Conway et al., 2005).

Working memory training components

Participants were required to execute the first training on 5 sequential days and the second training on 6 sequential days. Participants were free to choose where and when they executed the training during the training weeks, as long as they were able to concentrate fully on the tasks. The duration of the training was respectively 15 and 25 minutes per training session.

Training component 1

Reading Span Task. The Reading Span Task (RST: Daneman & Carpenter, 1980) measures the processing and storage functions of the WM (Shipstead et al., 2012), specifically participants' ability to shift between two tasks. These two tasks are: the memorization of a series of letters (F, H, J, K, L, N, P, Q, R, S, T, and Y) as well as judgment whether a sentence makes sense or not (e.g. The only furniture Steve had in his first bowl was his waterbed). The design of the test was the same as of the OST, with exception of the operations which were replaced by sentences. They had to judge whether the sentence made sense or not by clicking true or false on the screen. Half of these sentences did make sense. To train the WM of the experimental group the level of the task adapted to their WM. When participants judged the sentences correctly *and* recalled all letters in the correct order, the level increased with one letter and sentence. When they made an error on the sentence *and/or* letter part, they executed the same level again. The level ranged from 3 to 12. Conversely, the control group executed the same level – 3 –, independent of their performance. All participants received the same letter (2 items), sentence (15 items) and letter-sentence combination practice phase (2 items). The maximal reaction time to judge the sentences in the test phase was their average reaction time in the sentence practice phase plus 2.5 times the standard deviation. To make sure participants focused on both parts of the task we told them that we could only use data from participants who judged 85 percent of the sentences correctly. The high correlation with other valid WM tasks, like the SST and OST, shows that WM is an underlying construct of this test. Cronbach's alpha varies between .78 en .86 (Kane et al., 2004).

Training component 2

The second training component took place 5 months after training component 2.

Dual N-Back Task. The *n-Back Task* (Kirchner, 1958; Moore & Ross, 1963) is one of the most extensively used tasks to measure WMC (For a review, see Kane & Engle, 2002). In this study participants executed the dual *n-Back Task* (Jaeggi et al., 2007), which consisted of 13 trials of *n* + 20 auditory and visual stimuli. The aim of the participant was to continuously indicate whether the item matched the item that appeared *n* items ago in the string of stimuli. Auditory stimuli were 8 consonants (C, H, K, L, Q, R, S, and T) whereas the visual

stimulus was a blue square that could appear on 8 different locations regarding a white cross in the middle of the screen. The stimulus was presented for 500 ms with an inter-stimulus interval of 2500 ms. Participants were instructed to press in these 3000 milliseconds (ms) the L key when the auditory stimulus matched the *n*-back stimulus, the A key when they observed a letter match and both keys when both stimuli matched. Of the 20 experimental trials, 4 presented a square only, 4 presented a letter only, 2 presented both targets and 10 presented no targets at all. Participants trained their updating and shifting abilities with this task. For example, a two-back task required subjects to maintain the last seen 2 auditory as well as visual items in their WM and thus update their memory set with each new item and dropping out the least recent one. To train the WM maximally the training adapted to the level of the participant in the experimental group. The start level of *N* was 1 and this could range to 5. When participants made three errors or less on both the auditory and the visual part the level went one *n* up whereas five errors or more on one of the two parts resulted in a lower level. Participants continued on the same *n*-back level between these error ranges. The placebo group received the 0-back task, in which participants need to compare the stimuli with the first seen stimulus. In this way participants did not train their WM since the only cognitive process they used is their short-term memory to remember the first-seen stimulus.

Symmetry Span Task. In the Symmetry Span Task (SST: Kane et al., 2004) participants had to memorize the order and location of a set of squares while they judged the symmetry of images. This typical WM task measures the ability to shift and to cope with proactive interference. The instruction was to memorize the location of a red square in a 4 by 4 matrix and recall the location of these squares in correct order at the end of the trial by clicking them in the right order in the matrix. The squares were alternated by patterns of white and black squares in an 8 by 8 matrix of which participants had to judge the symmetry by clicking on the yes or no screen button when the question 'Is this symmetrical?' appeared. Half of these images were symmetrical. To train the WM of the experimental group optimally they received an adaptive training that increased with one level when they made no errors on both parts and continued on the same level when an error was made. They started with a set of 2 squares and could maximally receive 12 squares in 17 trials. Conversely, the placebo group's level was stable – 2 squares – over all 29 trials to prevent

training of their WM. Both groups could practice each part of the task. The experimental group received 2 times 2 and 2 times 3 squares whereas the placebo group received 5 times 2 squares. Secondly, they judged the symmetry of 15 images. Their average response time on this part plus 500 ms was used in the test phase. Lastly, both groups could practice the combination of the two parts of the task with 2 times 2 squares alternated with symmetry images. The reliability of the SST is high (Unsworth, Redick, Heitz, Broadway, & Engle, 2009), with an internal consistency of $\alpha = .86$ (Kane et al., 2004).

Procedure

The study and consent procedure was conducted in line with the Declaration of Helsinki, approved by the Ethical Committee of the Psychology department of the Erasmus University Rotterdam. Participants signed a digital informed consent before the first assessment. Written consent was obtained from caretakers of participants younger than 18. Figure 1 shows the assessment of the questionnaires, WM tasks and two training weeks during the year. They could perform all tasks and questionnaires from their own pc. The online tool Inquisit (Millisecond, Seattle, WA) was used for the WM tasks and training and Qualtrics (Qualtrics, Provo, UT) for the questionnaires. Participants filled in all questionnaires during each assessment, except the IES and UCL on the fourth assessment. We chose to shorten the questionnaire before the second training as much as possible to keep participants motivated to complete the second training. We chose to exclude the IES and UCL in that assessment because intrusions and coping style are relatively stable over time. Moreover, the IES is the most emotionally demanding questionnaire and the UCL is the longest one (Horowitz et al., 1979; Schreurs et al., 1993; Weiss & Marmar, 1997). Questionnaire 5 asked participants whether they had used a calculator or pen and paper to execute the WM tasks, to check for compliance to the regulations. Participants received their credits at the end of the study.

Results

We used mixed design analyses of variance (mixed ANOVAs) to explore the research question with group as between factor and the questionnaires and WM tasks on the

respectively 5 (questionnaires) and 6 (WM tasks) measurements as within factors[7]. Greenhouse-Geisser adjustments were used under violations of sphericity.

Time effects

Table 1 and 2 (see Appendix B and C) show that students overall changed significantly in their well-being during their first academic year. That is, their VAS scores show they became less sad and anxious and more cheerful and relaxed. This trend is reflected in their decreasing scores on the depression (BDI-II) and anxiety (STAI) scales. Surprisingly, their scores on the other anxiety scale, the TMAS, increased over time. Furthermore, their ruminative and intrusive thoughts, respectively measured with the RRS and IES, diminished as well. A reason for these positive results might be their changed coping style (UCL); they tackled problems more actively, were less passive, searched more for social support and were less avoidant. In addition, they became less stressed (PSQ). Interestingly, their attentional control (ACS) decreased and their decreased control was reflected in a rise of impulsive behavior (BIS-11).The WMC scores show mixed results. Overall, the scores of both groups on the DST ere table over time, but they became significantly better on recalling the letters of the OST. However, their scores on the math part of the OST significantly decreased.

Training effect on Transfer Working Memory Tasks

Digit Span Task

The experimental WM training did not lead to different scores on the DST compared to the control group on any of the DST scores when analyzing all 6 measurements: forward traditional score (F (3.97, 301.43) = 1.25, $p > .05$, *partial* $\eta^2 = .02$), forward maximal score (F (4.20, 315.09) = 1.45, $p > .05$, *partial* $\eta^2 = .02$), backward traditional score (F (4.11, 312.22) = .86, $p > .05$, *partial* $\eta^2 = .01$), and backward maximal score (F (3.55, 269.99) = .70, $p > .05$, *partial* $\eta^2 = .01$). Training WM did neither lead to an effect on the DST when analyzing the direct effect of both training components (see Table 3 in Appendix D).

[7] This article only describes the relevant analyses for answering the hypotheses.

Operation Span Task

Overall, the training did not influence the partial unit credit (PUC) score (percentage correctly recalled letters) compared with the control group when analyzing all 6 measurements: (F (3.15, 242.58) = .92, p > .05, *partial* η^2 = .01). Neither did they differ on the errors on the math part of the task: (F (4.29, 338.81) = 1.35, p > .05, *partial* η^2 = .02). Similar to the DST, no direct effect of training WM was found on the PCU score, nor on the math errors (see Table 3 in Appendix D and Table 4).

Table 4. Means (and standard deviations) of the training and placebo group on the operation span task measures

		Training component 1		Training component 2	
		Pre-training	Post-training	Pre-training	Post-training
Math errors	WM training	3.47 (3.02)	2.88 (2.62)	4.26 (4.29)	4.41 (4.18)
	Placebo training	3.48 (3.14)	4.37 (3.47)	4.25 (2.67)	4.57 (3.24)
PCU score	WM training	.86 (.13)	.88 (.13)	.88 (.12)	.82 (.21)
	Placebo training	.87 (.09)	.89 (.09)	.87 (.13)	.87 (.12)

Training effect on Questionnaires

The effect of training over all five (questionnaires) and six (WM tasks) measurements was explored with mixed design ANOVAs. To measure the direct effect of training, we executed contrasts comparing pre and post training data for both training components as well.

Against expectations, no interaction effect of the training was found on any of the different VAS measures: sad (F (3.71, 341.17) = .96, p > .05, *partial* η^2 = .01), anxious (F (2.92, 268.50) = 1.68, p > .05, *partial* η^2 = .02), cheerful (F (4, 368) = .89, p > .05, *partial* η^2 = .01), relaxed (F (4, 368) = .27, p > .05, *partial* η^2 = .00), and angry (F (3.52, 324.09) = 1.07, p > .05, *partial* η^2 = .01). The unchanged scores on the VAS scales represented the lack of effect of the training on the psychopathology scales. That is, the WM training did not lead to the expected stronger decrease in depression symptoms compared with the placebo training (BDI-II: F (2.88, 265.12) = .11, p > .05, *partial* η^2 = .00). Training WM did neither lead to a stronger decrease in anxiety symptoms compared with the placebo training on the STAI

total (F (3.31, 304.25) = .21, p > .05, *partial* η^2 = .00), trait (F (3.36, 306.81) = .53, p > .05, *partial* η^2 = .01) and state (F (3.50, 321.61) = .22, p > .05, *partial* η^2 = .00), and the TMAS (F (3.10, 281.89) = 1.44, p > .05, *partial* η^2 = .02). This is in line with the stable level of intrusion and avoidance symptoms of PTSD compared with the placebo training, measured with the IES (F (2.65, 256.64) = 1.60, p > .05, *partial* η^2 = .02). Nor did the training influence the level of rumination (RRS: F (3.15, 289.76) = .23, p > .05, *partial* η^2 = .00). Furthermore, their coping mechanisms remained stable (UCL total: F (2.46, 235.75) = 1.12, p > .05, *partial* η^2 = .01). Specifically, training WM did not lead to different coping styles than the placebo training: tackling problems actively (F (3, 288) = 2.12, p > .05, *partial* η^2 = .02), palliative reaction (F (2.62, 251.84) = 2.08, p > .05, *partial* η^2 = .02), avoidance (F (2, 288) = .27, p > .05, *partial* η^2 = .00), expressive support-seeking coping (F (2.54, 243.47) = .28, p > .05, *partial* η^2 = .00), passive coping (F (2.71, 260.07) = 1.48, p > .05, *partial* η^2 = .02), expression of emotions/anger (F (3, 288) = .46, p > .05, *partial* η^2 = .01), and comforting cognitions (F (2.58, 247.31) = 1.19, p > .05, *partial* η^2 = .01).

The training did neither lead to more self-control compared with the placebo training (BSCS: F (2.77, 254.84) = 1.00, p > .05, *partial* η^2 = .01), nor to less impulsivity (BIS-11: F (2.96, 272.54) = .30, p > .05, *partial* η^2 = .00), attentional control (ACS: F (3.25, 296.10) = .37, p > .05, *partial* η^2 = .00) and less stress (PSQ: F (2.71, 249.89) = .08, p > .05, *partial* η^2 = .00).

Mixed ANOVA contrasts (see Table 3 in Appendix D) show that there was neither a direct effect of the two training components on students' psychological well-being. The only significant effect was the decreased score on the coping style 'tackling problems actively' of the experimental group compared to the placebo group, after the second training component. Important to note is that the UCL was not measured directly before the training week, but eight weeks before the training (see Figure 1 in Appendix A).

Academic performance

To explore whether the training resulted in better academic performance in the WM training group we compared the difference in their marks between the courses before the training weeks (course 2 and7) and the exam right after the training weeks (courses 3 and 8) with that of the placebo group. Training WM did not lead to a change in marks on course 2 and 3 (t (118) = .48, p > .05, r = .04) or on course 7 and 8 (t (114) = -.69, p > .05, r = .06) compared with executing the placebo training.

Discussion

Previous studies show that training WM might improve cognitive functioning (e.g. Dahlin, Nyberg, Bäckmann, & Neely, 2008; Li et al., 2008; Loosli et al., 2012) as well as emotional functioning (e.g. Klingberg, 2005; Houben et al., 2011; Subramaniam et al., 2012) and self-control (Houben et al., 2011). The current study attempted to train students' WM with the aim to improve their functioning on those areas.

There is no effect of any of the two WM training components on participants' WMC, measured with two transfer WM tasks. The absent effects of training on psychopathology measures, like anxiety, depression, rumination, intrusions and stress and their coping style – except tackling problems actively – might be a consequence of the absent effect of the WM training on WMC. The same cause might be applied to the absent effect on academic performance, impulsivity and attentional control.

Independent of training, students became more relaxed and cheerful, less sad, anxious and stressed during the academic year. Furthermore, they ruminated less and had less intrusive thoughts. Moreover, their coping styles changed, which are generally quite stable (De Ridder & Schreurs, 2001). Two causes of this change are possible. Firstly, students' well-being changed positively during the academic year because they became accustomed to the required demands of the university. Secondly, training WM - independent of the level of training - resulted in improved psychological well-being.

In contrast to the present results, other studies did find that a WM training resulted in an increased WMC in healthy samples (e.g. Borella et al., 2010; Chein & Morrison, 2010; Thorell et al., 2009). The most straightforward explanation for the lack of differences in both groups is the notion that a WM training is not effective in improving WMC, levels of

psychopathological symptoms and academic performance. This explanation is confirmed by a recent study, which showed WM training did not lead to a reduction of rumination and depression, neither to an improved WM in students with heightened rumination scores (Onraedt & Koster, 2014). In addition, the studies of Jaeggi, Bushkuehl, Jonides and Perrig (2008) and Jaeggi and colleagues (2010) found only on a part of their transfer tasks near transfer whereas they did find far transfer of WM training to fluid intelligence. Melby-Lervåg and Hulme (2013) propose in their meta-analysis that the individual positive findings are due to the use of untreated control groups, which led to an overestimation of found transfer results of the experimental group. The failure to replicate these early positive findings might confirm this suggestion (Jaeggi, Buschkuehl, Jonides, & Shah, 2011; Bergman Nutley et al., 2011). Thus, an explanation of the current absent effect of WM training might be that WM training does not have that much impact as proposed by supporters of WM training.

However, alternative explanations cannot be ruled out and should be considered when interpreting the present lack of effect. Firstly, different WM training designs might influence the variation in effects. To decrease this variability in training designs Shipstead, Redick and Engle (2012) formulated several preconditions for a WM study design to validly measure the effect of WM training. Firstly, several transfer tasks are necessary to measure the effect of WM training on WMC. The current study meets this precondition, as we used two transfer tasks that both measure WMC. The second precondition indicates that short-term memory tasks need to meet two conditions to reflect participants' ability to recall information from outside STM instead of measuring immediate retention, as most short-term memory tasks do (Unsworth & Engle, 2006). Firstly, testing has to be continued regardless of the performance of the participant. In the current study we met this criterion partly since our participants all executed the total OST, independent of their score, but on the DST the level adapted to participants' performance. Secondly, partial credit scoring – assigning a credit for each recalled correct item – has to be applied when calculating short-term memory scores. This score reflects participants' ability to recall information from outside of STM instead of measuring immediate retention (Unsworth & Engle, 2007). We used a version of this scoring – partial-credit unit scoring (Conway et al., 2005) – to calculate scores of the OST. We did not apply this method on the DST but used the most employed

scoring method, which are the highest scores before two consecutive errors were made and the highest scores independent of errors. Shipstead's third precondition for a valid training study is the use of an active control group that executes an adaptive task as well, but which do not involve WM. Shipstead argues that an active control groups that executes a non-adaptive training – such as in our study – is among the best options currently executed. The last advice for a good WM study design is the avoidance of subjective measures since a number of studies (Aiken & West, 1990; Conway & Ross, 1984; DeLoache et al., 2010; Greenwald, Spangenberg, Pratkanis, & Eskenazi, 1991; Orne & Scheibe, 1964) showed that expectations can also cause a change on these measures. In WM studies, these expectations might be about the group they think they are in. Our study consisted of objective (WM tasks and marks) as well as subjective (self-report questionnaires) measures. As we wanted to measure the transfer of WM training on psychopathology, coping, academic functioning and self-control, in our view objective measures are impossible to implement because for the majority of these outcomes, no objective measures are available. Thus, regarding the preconditions of Shipstead the current study met two of the three preconditions partly. Therefore, it might be possible that this failure to meet all preconditions optimally is the cause of the absent effects.

Another alternative explanation for the lack of effect might be the short training duration. Klingberg (2010) stated that the total duration of a WM training must be at least 3 weeks or 8 hours. Our study participants were required to train 1.25 hours during the first WM training component and 2.5 hours in the second WM training component. This might have been too short to increase WMC. The reason for not implementing a longer training time were low compliance, experienced in former studies. Future research should investigate the influence of treatment duration on improvements in WMC.

A limitation of the current study is that 21.2% of the experimental group – compared to 7.4% of the placebo group – confessed they used aids during the tests or training. This might have influenced the results. However, even when the use of aids influenced the results it did not lead to significant differences between the groups. A possibility to avoid these influences might be to test participants in presence of an experimenter. However, when a large sample has to train in the laboratory every day, time

and motivation issues of the sample will probably lead to a high drop-out. Moreover, other training studies in depressed and anxious patients of our lab show that the possibility to train from home is one of the most valued characteristics of the design.

In sum, training participants' WM did neither lead to an improved WMC and academic performance nor to improved psychological well-being. This might be an indication that WM training cannot solidly increase WMC, although alternative explanations cannot be ruled out. Nevertheless, as there are still many positive findings regarding WM training in clinical populations it might be useful to explore the effect of WM training factors on WMC, like the timeline of training and assessments (e.g., length of training sessions, overall duration of training period, number of assessment sessions), conditions of assessment (e.g., comfort and location of assessment, encouragement level by lab staff) as well as the setting of training (e.g., laboratory, school, home).

Appendix A

Questionnaires 1 + WM tasks 1	WM tasks 2	Training component 1	Questionnaires 2 + WM tasks 3	Questionnaires 3 + WM tasks 4	Questionnaires 4 (except IES and UCL) + WM tasks 5	Training component 2	Questionnaires 5 + WM tasks 6

Figure 1. Overview of the assessment of questionnaires, working memory tasks and training components during the academic year

Appendix B

Table 1. Time effects of working memory tasks, self-report questionnaires and academic performance

Variable	*Df*	*F*	*p-value*	*Partial η²*
Forward traditional score	3.97, 301.43	1.90		.02
Forward maximal score	4.20, 315.09	.17		.00
Backward traditional score	4.11, 312.22	.69		.01
Backward maximal score	3.55, 209.99	1.29		.02
Operation Span PCU score	3.15, 242.58	2.76	*	.04
Operation Span math errors	4.29, 338.81	2.95	*	.04
VAS sad	3.71, 341.17	8.46	***	.08
VAS anxious	2.92, 268.50	11.20	***	.11
VAS cheerful	4, 368	5.62	***	.06
VAS relaxed	4, 368	5.93	**	.06
VAS angry	3.52, 324.09	1.61		.02
BDI-II	2.88, 265.12	40.34	***	.31
STAI total	3.31, 304.25	14.66	***	.14
STAI trait	3.34, 306.81	14.10	***	.13
STAI state	3.50, 321.61	10.70	***	.10
TMAS	3.10, 281.89	14.83	***	.14
IES	2.65, 256.64	16.66	***	.15
RRS	3.15, 289.76	17.88	***	.16
UCL total	2.46, 235.75	1.07		.01
UCL tackling problems actively	3, 288	2.54		.03
UCL palliative reaction	2.62, 251.84	1.37		.01
UCL avoidance	3, 288	3.28	*	.03
UCL expressive support-seeking	2.54, 243.47	6.58	**	.06
UCL passive coping	2.71, 260.07	10.49	***	.06
UCL expression of emotions/anger	3, 288	.15		.00
UCL comforting cognitions	2.58, 247.31	.98		.01
BSCS	2.77, 254.84	2.76	*	.03
BIS-11	2.96, 272.54	4.98	**	.05
ACS	3.25, 296.10	6.21	***	.06
PSQ	2.72, 249.89	14.61	***	.14
Academic performance	5.64, 1166.58	47.83	***	.19

Note: * *p<.05*, ** *p<.01*, *** *p<.001*

Appendix C

Table 2. Means (and standard deviations) of self-report questionnaires significant over time

Variable	Time 1	Time 2	Time 3	Time 4	Time 5
VAS sad	22.48 (23.53)	14.54 (19.94)	10.33 (15.35)	16.77 (23.34)	9.68 (15.99)
VAS anxious	13.91 (18.50)	7.38 (14.09)	5.34 (11.64)	8.57 (15.27)	2.96 (4.60)
VAS cheerful	50.46 (23.42)	59.57 (23.84)	57.39 (23.27)	50.46 (28.21)	59.18 (26.20)
VAS relaxed	54.44 (27.86)	65.63 (24.43)	65.74 (23.83)	55.86 (27.56)	64.97 (27.60)
BDI-II	9.24 (6.49)	5.67 (6.67)	4.35 (5.53)	4.64 (6.07)	3.48 (5.10)
STAI total	73.97 (18.37)	67.72 (18.46)	63.77 (15.73)	69.19 (19.93)	65.00 (16.78)
STAI trait	38.05 (9.68)	34.95 (10.24)	32.82 (8.59)	34.49 (9.83)	33.73 (9.43)
STAI state	35.91 (10.13)	32.78 (9.32)	30.95 (8.05)	34.70 (10.79)	31.27 (8.63)
TMAS	32.73 (4.79)	33.32 (4.70)	34.58 (4.41)	34.01 (4.56)	34.96 (4.55)
IES	18.21 (17.22)	10.99 (14.79)	10.55 (13.93)		9.04 (13.96)
RRS	45.67 (12.34)	39.98 (11.38)	38.57 (11.23)	40.44 (11.55)	38.60 (11.63)
UCL avoidance	17.11 (3.11)	17.06 (3.46)	17.07 (3.33)		16.27 (3.68)
UCL expressive support-seeking	14.60 (3.83)	15.20 (3.73)	15.81 (3.86)		15.49 (3.75)
UCL passive coping	13.11 (3.44)	12.64 (3.72)	11.80 (3.27)		11.78 (3.25)
BSCS	43.13 (9.32)	44.54 (8.31)	44.69 (9.08)	43.83 (8.63)	44.34 (8.71)
BIS-11	59.38 (9.95)	60.33 (10.21)	58.24 (9.62)	60.50 (10.69)	60.00 (10.84)
ACS	50.17 (8.46)	52.32 (8.70)	52.39 (8.13)	51.67 (8.13)	52.58 (8.86)
PSQ	64.12 (15.27)	60.01 (15.51)	56.60 (15.08)	58.24 (14.93)	57.51 (15.58)

Appendix D

Table 3. Mixed ANOVA contrasts representing effects of training component 1 and 2

		Training component 1			Training component 2		
Variable	*Df*	*F*	*p-value*	*Partial η²*	*F*	*p-value*	*Partial η²*
Forward traditional score	76	.58		.01	.28		.00
Forward maximal score	75	1.06		.01	.05		.00
Backward traditional score	76	1.07		.01	.09		.00
Backward maximal score	76	.82		.01	.10		.00
Operation Span PCU score	77	.00		.00	2.13		.03
Operation Span math errors	79	2.53		.03	.00		.00
VAS sad	92	.71		.01	1.90		.02
VAS anxious	92	1.99		.02	.00		.00
VAS cheerful	92	.04		.00	.16		.00
VAS relaxed	92	.31		.00	.41		.00
VAS angry	92	.54		.01	1.42		.02
BDI-II	92	.26		.00	.00		.00
STAI total	92	.11		.00	.49		.01
STAI trait	92	.22		.00	.06		.00
STAI state	92	.02		.00	.72		.00
TMAS	91	.52		.01	2.21		.02
IES	97	3.52		.04	.01		.00
RRS	92	.14		.00	.16		.00
UCL total	96	.66		.00	3.15		.03
UCL tackling problems actively	96	.53		.01	4.12	*	.04
UCL palliative reaction	96	3.37		.03	3.23		.03
UCL avoidance	96	.70		.00	.04		.00
UCL expressive support-seeking	96	.31		.00	.49		.01
UCL passive coping	96	.13		.02	2.68		.02
UCL expression of emotions/anger	96	.80		.01	.11		.01
UCL comforting cognitions	96	2.76		.01	.01		.01
BSCS	92	.26		.00	3.09		.03
BIS-11	92	.21		.00	.80		.00
ACS	91	.27		.00	.01		.00
PSQ	92	.79		.00	.76		.00

Note: * *p<.05*, ** *p<.01*, *** *p<.001*

Chapter 7|

Decreasing Dysphoric Thoughts by a Working Memory Training

This chapter has been submitted for publication as: Wanmaker, S., Hopstaken, J.F., Asselbergs, J., Geraerts, E., & Franken, I.H.A. (submitted). Decreasing dysphoric thoughts by a working memory training: A randomized double-blind placebo-controlled trial.

Abstract

Depressive symptoms are related to deficient executive functioning, in particular working memory. Previous findings show that working memory capacity (WMC) can be increased by training and this diminishes symptoms of psychopathology. The current study explored by means of a double-blind randomized controlled trial whether a gamified WM training could reduce symptoms of depression, anxiety, and rumination in a sample of 61 dysphoric students. Moreover, WMC and psychopathology were compared to a healthy control group. WM training resulted in a larger WMC compared to the placebo training and compared to healthy students, but not in a decrease of psychopathological symptoms. We discuss potential explanations for these findings.

Depression negatively affects health (Barth, Schumacher, & Herrmann-Lingen, 2004; Knol et al., 2006), personal relationships (Fröjd et al., 2008), and productivity (Doris, Ebmeier, & Shajahan, 1999). In students depression is associated with lower educational performance (DeRoma, Leach, & Leverett, 2009; Fröjd et al., 2008; Hysenbegasi, Hass, & Clayton, 2005) and higher drop-out rates from education (Lecompte, Kaufman, Rousseeuw, & Tassin, 1983; Szulecka, Springett, & De Pauw, 1987). Especially ruminating about a dysphoric mood is associated with difficulties in concentration (Lyubomirsky, Kasri, & Zehm, 2003), complex problem solving (Lyubomirsky et al., 2003; Lyubomirsky & Nolen-Hoeksema, 1995), and impaired work strategies (Lyubomirsky et al., 2003). Thus, depression and rumination interfere with cognitive functions that are essential for academic and job performance. Extensive empirical research shows these cognitive impairments are related with reduced working memory (WM) functioning (e.g. De Lissnyder et al., 2012; Owens & Derakshan, 2013).

WM is a multi-component system which temporarily stores, activates and maintains information in its limited capacity. This memory component is essential for cognitive functions including allocation of attention, strategy selection, planning, reasoning, and learning (cf. Baddeley, 1992). Several separable key processes support efficient functioning of WM (Jonides et al., 2008; Miyake & Shah, 1999; Nee & Jonides, 2008). Depressive individuals show impairment in these processes. Particularly, depression results in an impaired ability to remove negative information from WM once it has entered (Joormannn & Gotlib, 2008; Levens & Gotlib, 2010; Whitmer & Banich, 2007). In addition, depressive individuals have difficulties in shifting between negative and positive information (Harvey et al., 2004; Rogers et al., 2004), which manifests in a bias for negative information (Murphy et al., 1999). Furthermore, their ability to inhibit irrelevant information is reduced (Lemelin et al., 1996; MacQueen, Tipper, Young, Joffe, & Levitt, 2000; Monsell, 1996; Trichard, et al., 1995). Depression symptoms, like difficulties in learning (Grossman, Kaufman, Mednitsky, Scharff, & Dennis, 1994; Porter, Gallagher, Thompson, & Young, 2003; Zakzanis, Leach, & Kaplan, 1998), attention (Moritz et al., 2001; Porter et al., 2003; Zakzanis et al., 1998), concentration (Zakzanis et al., 1998), decision-making (Murphy et al., 2001) and planning (Beats, Sahakian, & Levy, 1996; Elliott et al., 1996; Moritz et al., 2001), are expressions of WM deficits as WM controls all these functions. A study of Owens,

Stevenson, Hadwin, and Norgate (2012) demonstrated worry and WM mediated the relation between negative affect and academic performance. These findings show that an efficient WM is essential for both psychological well-being and academic performance.

Currently, the effects of training WM are heavily debated. There are some initial promising findings show WM training can increase working memory capacity (WMC) and diminish symptoms of various disorders (Houben, Wiers, & Jansen, 2011; Klingberg, 2010; Subramaniam et al., 2012; Vogt et al., 2009; Westerberg et al., 2007). Critics, on the other hand, indicate that results regarding generalization of WM training to other skills are mixed (Melby-Lervåg & Hulme, 2013; Shipstead, Redick, & Engle, 2012; 2013). However, as the results are generally positive, and there are many advantages of computer training, such as high efficiency, cost-effectiveness, and easy accessibility, it is worth further exploring the effect of training WM. Research regarding effects of WM training in depression is relatively recent. Most studies use students with dysphoria, a subclinical form of depression (Joormann & Gotlib, 2010). Owens, Koster, and Derakshan (2013) studied dysphoric students and found gains in WMC due to WM training at both behavioral and neural assessments. However, the training had no effect on self-reported depression. In the study of Onraedt and Koster (2014) training performance improved, but did not transfer to WM on non-trained WM tasks, nor did it decrease rumination or depression in high ruminators. Results regarding WM training in dysphoric individuals are thus scarce and mixed, which amplifies the need for further exploration of training possibilities in this sample.

One of the essential factors for a successful training program is constant engagement with the tasks (Shipstead et al., 2012). This can be reached by using a level that is neither boring nor too challenging (Shipstead et al., 2012) and by the addition of game elements (Prins, Dovis, Ponsioen, Ten Brink, & Van der Oord, 2011). For instance, Prins and colleagues (2011) showed game elements positively influenced motivation, compliance and performance during training and resulted in a better WM in children with ADHD. The inclusion of game elements thus might be an important factor to increase efficacy of WM training in dysphoric samples. Therefore the aim of the current study was to train WM of dysphoric students by a gamified WM training. Dysphoric students were double-blind randomly allocated to a WM or placebo training. We measured them before

and after the nine session training on self-reported depression, anxiety and rumination, as these psychopathology are all related to WM impairments (De Lissnyder et al., 2012; Owens & Derakshan, 2013; Eysenck, Derakshan, Santos, & Calvo, 2007). Moreover, we compared the groups with a healthy control group on the pre-test to study whether they differed in WMC before and after training WM. As Jaeggi, Buschkuehl, Jonides, and Perrig (2008) found that the number of completed training sessions was related to the level of change in WMC, we also explored whether this was the case in our study. Overall, we expected that dysphoric students' WMC was diminished compared to that of their healthy counterparts. Furthermore, we hypothesized that a gamified WM training would result in an increased WMC and reduction of depression, anxiety and rumination in our dysphoric sample, which would decrease the gap between the dysphoric and healthy students. The level of change in WMC and psychopathology in the experimental group was expected to be dependent of the number of training sessions.

Method

Participants

Sixty-one dysphoric psychology students participated in the study. They were, based on subject number, randomly double-blind allocated to the experimental (n = 34) and placebo training group (n = 27). Moreover, these groups were compared with a healthy control group (n = 21) on all measures of the pre-test (see Figure 1). The inclusion criterion was a Beck Depression Inventory (Beck, Steer, & Brown, 1996) score of minimally 10 for the dysphoric group and of maximally 5 for their healthy counterparts. The three groups did not differ in the percentage men (χ^2 (2) = .04, p > .05), students with a Dutch nationality (χ^2 (2) = .43, p > .05), and age (H (2) = 2.07, p > .05). We excluded the healthy control group in the analyses regarding medication and therapy, as that information was only relevant for the further analyses of both dysphoric groups. Those two groups did not differ in the percentage students currently following therapy (see Table 1; χ^2 (1) = 3.36, p > .05), history of therapy (χ^2 (1) = .09, p > .05) and use of medication for their psychopathological complaints (χ^2 (1) = .60, p > .05).

Groups	Pre measurement	Training	Post measurement
Experimental training group	*n* = 35 Drop outs (*n* = 1): did not meet the inclusion criteria anymore	Experimental training	*n* = 26 Drop outs (*n* = 8): Did not train (*n* = 6) Quit university (*n* = 2)
Placebo training group	*n* = 34 Drop outs (*n* = 7): did not meet the inclusion criteria anymore	Placebo training	*n* = 22 Drop outs (*n* = 5): Did not train (*n* = 3) Training did not work (*n* = 1) Executed partly the experimental training (*n* = 1)
Healthy control group	*n* = 25 Drop outs (*n* = 4): did not meet the inclusion criteria anymore	N/A	N/A

Figure 1. Test procedure

Table 1. Demographic variables

Variable	Experimental group	Placebo group	Healthy control group
Gender (% men)	24.2	22.2	23.8
Nationality (% Dutch)	84.9	88.9	90.5
Age (*M*, *SD*)	20.58 (3.87)	20.96 (3.26)	21.43 (4.70)
% Current therapy	6.1	22.2	0.00
% History of therapy	33.3	37.0	0.00
% Use of medication for psychopathology	7.4	3.0	0.00

Measures

Working Memory

Spanboard Task. WM performance was measured using a computerized version of the Spanboard task adapted from Prins and colleagues (2011). The user is shown a 4 x 4 grid consisting of 16 blue squares. The squares light up in a random order, one after the other. At the end of the trial the user has to replicate the sequence by selecting the squares in the correct order. The first sequence consists of three squares and after two consecutive completions the sequence increases by one square. If the user fails to replicate two consecutive sequences the task ends and the number of squares of the last successful sequence represents their memory span. The participant first receives a few practice trials. When the participant correctly replicates two consecutive practice trials the actual test starts. Each square lights up for 900 milliseconds and it takes 500 milliseconds for the next square to light up.

Psychopathology

Depression. The Beck Depression Inventory – II (BDI-II; Beck, Steer, & Brown, 1996; Dutch version; Van der Does, 2002) measures participants' severity of depression symptoms. This self-report questionnaire contains twenty-one groups of statements about depression symptoms experienced the last two weeks. Adding up the scores of the questions, which range from 0 to 3, results in the total score. The reliability of this widely used questionnaire is good (Evers, Van Vliet-Mulder, & Groot, 2005), with a Cronbach's α of .94 in the present study.

Anxiety. The State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983, Dutch version; Van der Ploeg, Defares, & Spielberger, 1979) measures self-reported state and trait anxiety. Both subscales consist of 20 items with a scale ranging from 1 to 4. After pooling some items, both subscale total scores were used in the analyses. The psychometric qualities of the STAI are good (Bieling, Antony, & Swinson, 1998), with a Cronbach's α of .97 in the state part and .96 in the trait part in this study.

Rumination. The Ruminative Response Scale (RRS; Nolen-Hoeksema & Morrow, 1991, Dutch version; Raes, Hermans, & Eelen, 2003) measures the frequency of self-reported rumination behavior in 22 questions. Answer options range from 1 (*never*) to 4 (*always*),

summing up to the total score. The questionnaire shows sufficient reliability (Raes et al., 2009), which is confirmed by a Cronbach's α of .95 in the present study.

Training paradigm

Participants were required to play the WM training three times a week during three weeks. Each session lasted about 30 minutes. The experimental group (M = 9.10, SD = 3.61) and placebo group (M = 9.08, SD = 1.64) did not differ in the number of training sessions (range 6 – 17; U = 390.50, z = .55, p > .05, r = .07). The training program can be characterized as a role playing game where the user is free to walk around in a virtual two dimensional world. The user is represented by a character with different attributes, like strength and health-points. By defeating enemies the character earns experience points, gold and ability points, which he/she can use to buy better weapons and to become stronger. In the training area the user can choose freely which WM task to undertake. The player then enters a battle screen, consisting of a battle scene on the top half and the WM task at the bottom half of the screen. When the task is completed successfully the character damages the enemy; if the task is unsuccessful, the attack fails. The enemies in the training area are manipulated in such a way that their strength is always related to the strength of the user. Hence when the player becomes stronger so do the enemies, ensuring that it always takes four to five correct trials to defeat the enemy.

Throughout the training also the difficulty of the WM tasks were adjusted according to the performance level of the user. Whenever a user was successful on four consecutive trials the difficulty of the task went up by one. When the player was unsuccessful on two consecutive trials the difficulty of the task decreased by one. To prevent learning effects in the placebo condition, the difficulty of the tasks did not vary and had a low difficulty level of only two items that had to be remembered each trial.

The main objective of the game is to challenge for the title by defeating all of the 15 opponents in the tournament. The opponents in the tournament all have a fixed strength-level, and the opponents become stronger the further one gets into the tournament. Since the opponents become harder to defeat, it is imperative to level up one's character and become stronger by defeating the enemies in the training area. In essence, the user is free

to choose which WM task they wish to undertake in the training area. However to promote variety in the chosen tasks, certain in-game rewards were added to the game. For instance users received extra gold if they completed each WM task five times.

Training tasks

Simon task. This task is similar to the game Simon and can be used to measure working WM (e.g. Gendle & Ransom, 2006). The training adopts two versions of the Simon task. The first version consists of a ring divided in four colors (green, red, yellow and blue). The colors light up in random order and the user has to repeat the sequence in the correct order. In the second version of this task the sequence starts out with only one color and the user has to repeat this color. If successful, another color lights up and the user has to add this color to the previous sequence, followed by repeating the whole sequence. The difficulty of the task depends on the performance of the participant with a minimum sequence length of three and a maximum of nine.

Symmetry span. The symmetry span is frequently used to measure WM (Kane et al., 2004). First, users see an 8 x 8 picture, consisting of 64 black and white squares, for 5500 milliseconds, followed by a question if the picture was symmetrical on the y-axes. The user has 5000 milliseconds to click on the yes or the no button. Then one square in a 4 x 4 grid lights up for 1500 milliseconds. At the end of the trial the user has to reproduce the sequence of squares by selecting them in the correct order. The difficulty of the task depends on the performance of the user with a minimum sequence length of two and a maximum of eight.

Operation span. In this version of the operation span (Unsworth, Heitz, Schrock, & Engle, 2005), participants first see a math problem (e.g. (1*2) + 1 = ?) for 5500 milliseconds. After the math problem participants have 5000 milliseconds to judge whether the answer on the screen was true or false by selecting one of these options on the screen. Then a letter (F, H, J, K, L, N, P, Q, R, S, T, and Y) appears on the screen for 1500 milliseconds. At the end of the trial participants have to recall the letters by selecting them in correct order in a 4 x 3 matrix containing all possible letters. The difficulty of the task depends on the performance of the user with a minimum sequence length of two and a maximum of eight.

Number recall task. Another task that is often used to measure WM is the number recall task (e.g. Cowan, 2001; Alloway & Alloway, 2010). The training adopts two versions of this task. In the first version the user hears a sequence of random numbers, ranging from 0 to 10. The user has to repeat the sequence, by typing in the numbers in the correct order. In the second version the user has to repeat the sequence as well, but in reverse order. The difficulty of the task depends on the performance of the user with a minimum sequence length of three and a maximum of nine.

Figure task. In this self-designed task a number of random colored figures (blue, red, green, purple, yellow, black, orange and white; square, circle, triangle, cross, star, question mark and exclamation mark) are depicted on the screen. The user has to remember the figures and is then asked what the color of a certain figure was. The difficulty of the task depends on the performance of the user and had a range from 3 to 7 figures and 7 to 24 seconds to study the figures.

Procedure

The study was approved by the Medical Ethical Committee of Rotterdam and registered at ClinicalTrials.gov (ID: NCT02184481). Students subscribed for the study via the psychology website and received credits for participation. The current experiment was part of a larger study about WM. As all participants received the same procedure, this will not have influenced the results of this study. Both the healthy and dysphoric group performed the pre-test at the laboratory of the university, which consisted of the transfer WM task and the psychopathology questionnaires. The dysphoric groups received a link to the training and a manual. The training had to be completed three times a week during three weeks on a Windows computer. The experimenter called them every week to monitor and discuss their progress. One week after they finished the training they completed the WM tasks and psychopathology questionnaires of the post-test.

Results

The dysphoric and healthy students were compared on the measures of the pre-test with an independent t-test for normally distributed data and exact Mann-Whitney tests for non-normally distributed data. The same analyses were used to explore whether the experimental training group was comparable to the healthy control group after the training. To measure the effect of training, data were submitted to mixed design analyses of variance (ANOVA). Each mixed ANOVA included one between-subjects factor for Group (WM training vs. placebo training) and Time (pre - post) as within-subject factor. Only relevant analyses to answer the research question are reported, that is; interaction effects (Group x Time) and Time (pre - post) effects. The significance level was set at .05 for all analyses.

Healthy control group – dysphoric group

As expected, the dysphoric group reported significantly more psychopathological complaints (see Table 2). That is, they were more depressed (U = 1260.00, z = 6.81, p < .01, r = .76) and suffered from more state (t (76.78) = -16.17, p < .01, r = .88) and trait anxiety (U = 1257.00, z = 6.76, p < .01, r = .75), which mirrored their higher total STAI score (U = 1256.00, z = 6.75, p < .01, r = .75). Furthermore, they ruminated more (U = 1224.00, z = 6.41, p < .01, r = .71). Interestingly, the dysphoric groups (*Mdn* = 5) did not differ in their WMC from the healthy control group (*Mdn* = 5), measured with the Spanboard task (U = 600.00, z = .12, p > .05, r = .01).

Working memory training effect

As intended with the WM training the experimental group's WMC increased more from pre to post measurement than that of the placebo group, measured with a transfer task (see Table 2 and 3). However, this increased capacity did not lead to a larger improvement of psychopathological complaints (see Table 2 and 3). That is, training WM did not have any effect on depression, anxiety and rumination. As seen in other studies, the complaints did decrease over time (see Table 3).

To explore whether the experimental WM training increased their WMC and decreased psychopathology to the extent of the healthy control group we compared the post scores on the WM measure and psychopathology of the experimental group with the

scores of the healthy control group. Training WMC with the experimental training resulted in a better WMC than that of the healthy control group (see Table 2; $U = 130.00$, $z = -2.38$, $p < .05$, $r = -.37$). Unfortunately, this effect on WMC did not transfer to their psychopathology; the experimental group was still more depressed (see Table 2; $U = 0.00$, $z = -5.91$, $p < .01$, $r = -.86$), reported more state ($t(31.64) = 9.95$, $p < .01$, $r = .87$), trait ($U = 0.50$, $z = -5.84$, $p < .01$, $r = -.85$) and total anxiety ($t(31.13) = 11.64$, $p < .01$, $r = .90$), and ruminated more ($U = 25.50$, $z = -5.30$, $p < .01$, $r = -.77$).

Table 2. Mean and standard deviations of working memory and psychopathology measures per group

		Pre training		Post training	
	Healthy control group	Experimental group	Placebo group	Experimental group	Placebo group
Spanboard	5.32 (1.06)	5.16 (.95)	5.57 (.90)	6.05 (.95)	5.43 (.60)
BDI-II	.63 (.96)	18.91 (6.86)	21.43 (8.00)	13.81 (9.24)	14.82 (10.48)
STAI total	46.42 (5.79)	98.53 (14.94)	101.09 (20.42)	88.23 (17.30)	89.91 (24.88)
STAI state	23.05 (2.91)	46.09 (9.70)	49.00 (10.63)	41.27 (8.67)	42.82 (12.69)
STAI trait	23.37 (3.25)	52.44 (8.18)	52.09 (10.88)	46.96 (10.13)	47.09 (13.23)
RRS	30.42 (6.25)	57.47 (11.84)	58.13 (13.59)	57.08 (15.06)	53.00 (14.94)

Table 3. Effect of working memory training on working memory and psychopathology measures

Measure	Analysis	*Df*	*F*	*P*	*Partial* η^2

Spanboard	Time	1, 41	8.98	< .01	.18
	Time x Group	1, 41	8.98	< .01	.18
BDI-II	Time	1, 46	44.12	< .01	.49
	Time x Group	1, 46	.63	Ns	.01
STAI total	Time	1, 46	19.09	< .01	.29
	Time x Group	1, 46	.55	Ns	.01
STAI state	Time	1, 46	11.40	< .01	.20
	Time x Group	1, 46	.82	Ns	.02
STAI trait	Time	1, 46	19.54	< .01	.30
	Time x Group	1, 46	.09	Ns	.00
RRS	Time	1, 46	2.97	Ns	.06
	Time x Group	1, 46	1.09	Ns	.02

Regression

To explore whether the number of completed training sessions was related to the level of change in psychopathology and WMC due to the WM training we used linear regression analyses using standardized values comparing the WM and placebo training. The difference scores (pre minus post) of the psychopathology scales and the Spanboard task subscales were the dependent variables and the number of completed training sessions was the predictor. Unexpectedly, a higher number of training sessions was not more predictive for changes in psychopathology or WMC in the experimental group than in the placebo group (all R^2's < .21, B's < .75, *p's* > .05).

Discussion

This study was set up to examine whether a gamified WM training would increase WMC and reduce depression, anxiety and rumination in dysphoric students. Furthermore, we explored whether their WMC differed of healthy students' WMC and whether training WM would diminish that gap. In line with our hypotheses, the dysphoric group reported significantly more psychopathological symptoms than the healthy control group. However, the groups did not differ in their WMC. Nevertheless, the WM training increased WMC to a larger extent than the placebo training did and resulted in an even higher WMC compared to the healthy students which did not execute any training. This gain in WMC was not transfered to self-reported symptoms of depression, anxiety and rumination and the

difference in these symptoms between healthy and dysphoric students remained.

The finding that dysphoric and healthy students did not differ in WMC before the intervention is in line with a significant number of other studies (Barch, Sheline, Csernansky, & Snyder, 2003; Grant, Thase, & Sweeney, 2001; Sweeney, Kmiec, & Kupfer, 2000). Cognitive deficits seem to be minimal in young individuals with mild depressive symptoms (Barch et al., 2003; Grant, et al., 2001), and characterize especially elderly depressed people and severely depressed inpatients with psychotic features (Grant et al., 2001). Furthermore, neuropsychological functioning depends on the severity of this disorder (e.g. Cohen, Weingartner, Smallberg, Pickar, & Murphy, 1982; Elderkin-Thompson et al., 2003; Ravnkilde et al., 2002). Our sample reported only minor depressive symptoms according to the categorization of Beck and colleagues (1996) and compared to some of the other studies that used dysphoric students (Owens & Derakshan, 2013; Owens et al., 2013). Their relatively low depression score might explain the absent difference in WMC between them and their healthy fellow students. Another explanation for this lack of difference is our use of a challenging WM task that required full engagement of participants. Several studies (Hertel, 1998, 2004; Joormann, Nee, Berman, Jonides, & Gotlib, 2010) show the difference in WM between healthy and depressed individuals is more evident when using relatively easy tasks. Easy tasks do not require participants to fully engage with the task and do not control participants' attention, thus allow rumination and mind wandering and therefore, are susceptible to individual differences in cognitive control and in the use of effective strategies. Future research could further explore whether WM deficits are indeed present in university students with dysphoria. As this sample is often used in research, results might not be representative for depressed individuals in general.

When focusing on the effect of WM training, the gain in WMC seems promising. This result is consistent with other studies showing WMC can be increased (Jaeggi et al., 2008; Klingberg et al., 2005; Olesen, Westerberg, & Klingberg, 2004). Although WMC increased, the transfer effects on psychopathology were absent. This pattern of results is seen in the study of Owens and colleagues (2013) as well. The effects of WM training are heavily debated, as the results are quite inconsistent. Some studies find an increase of both

WMC and far transfer measures (e.g. Klingberg et al., 2005; Prins et al., 2011). Remarkably, other studies find an effect on far transfer measures, without WMC improvement (Bickel, Yi, Landes, Hill, & Baxter, 2011; Dahlin, Nyberg, Bäckman, & Neely, 2008; Jaeggi et al., 2008; Jaeggi et al., 2010; Li et al., 2008; Schweizer, Grahn, Hampshire, Mobb, & Dalgleish, 2013). Another category of studies does not find any result on both WMC and far transfer measures (e.g. Onraedt & Koster, 2014; Redick et al., 2013). Redick and colleagues (2013) aimed to explore the efficacy of WM training using the best and most valid possible method, by taking all preconditions into account (Shipstead et al., 2012; Klingberg, 2010). That is, using both a no-contact control group and an active placebo-control group, using multiple valid measures of each construct, the inclusion of behavioral measures, and using a diverse sample. They found practice effects and a high level of statistical power, but still no effect of WM training on fluid intelligence, multitasking, WMC, crystallized intelligence, and perceptual speed. As the results are very contradicting, more studies like the current study are needed in order to draw firm conclusions about the efficacy of WM training.

Despite the lack of training effect, both groups' complaints decreased over time. This decline might be explained by the natural course of depression and anxiety symptoms (Kruijshaar et al., 2005; Ramsawh, Raffa, Edelen, Rende, & Keller, 2009; Spijker et al., 2002). Unexpectedly, a higher number of training sessions was not more predictive for changes in psychopathology or WMC in the experimental group than in the placebo group. This lack of influence of training duration might indicate that none of the two trainings – placebo nor WM training – does contribute to this improvement.

For a full interpretation of the result we have to mention some limitations of this study. Firstly, participants were dysphoric students with a relatively low level of depression (Beck et al., 1996). For practical and ethical reasons we first would like to explore the efficacy of this treatment in this sample instead of severely depressed adults. As little research compared depression and dysphoria (Gotlib and Joormann, 2010), it might be that the current results cannot be generalized to depressed individuals. Secondly, we measured WMC using only one task instead of the recommended multiple measurements by Shipstead and colleagues (2012). Performance on tasks can be influenced by numerous

factors (Redick et al., 2013) and thus, a recommendation for future research is to use multiple WM tasks to validly conclude about the effect of training on WMC.

In sum, a gamified WM training increased WMC in a dysphoric sample but this did not transfer to a decrease of depression, anxiety, and rumination. These changes in WMC or psychopathology were not dependent of the number of training sessions completed. However, both groups' complaints decreased over time whether WMC was challenged or not. Interestingly, WM training increased dysphoric students' WMC to such extent it was larger than that of the healthy control group.

Chapter 8|

General Discussion and Summary

Background

Previous findings show that a reduced working memory capacity (WMC) might underlie psychopathology (Ambrose, Bowden, & Whelan, 2001; Bolla, Brown, Eldreth, Tate, & Cadet, 2002; Cisler & Koster, 2010; Demeyer, De Lissnyder, Koster, & De Raedt, 2012; Jovanovski, Erb, & Zakzanis, 2005) and stress (Klein & Barnes, 1994). The present dissertation examined whether it is possible to reduce the negative consequences of these WM deficits by increasing one's WMC. Firstly, we examined whether a high WMC can protect against depressive feelings and a negative interpretation bias (chapter 2). In addition, we studied whether WM training is able to increase WMC and by doing so, reduce symptoms of depression, anxiety, and rumination in individuals with an anxiety or depression diagnosis (chapter 3 and 4) and a subclinical (chapter 7) sample. Furthermore, the efficacy of WM training on substance use and related factors, such as craving, impulsivity, attention bias for substance related cues, and psychopathology was investigated in substance use disorder (SUD) inpatients (chapter 5). Lastly, we explored the effect of training WM in healthy students' academic performance, stress, attentional and self-control, impulsivity, intrusions, rumination, symptoms of anxiety and depression, and coping abilities (chapter 6). The hypotheses underlying these five studies exploring the efficacy of WM training suppose that training WM increases WMC and therefore, positively affects behavior related to WM functioning. That is, we expected that an increased WMC would reduce psychopathology, substance use, craving, impulsivity, attention bias, intrusions, and stress and improve academic performance, attentional and self-control, and coping abilities. In this chapter the main findings of the studies are discussed and reviewed. Furthermore, we address clinical implications and directions for future research. Figure 1 summarizes the designs, measures and effects of the WM training effect studies.

Loading WM

As WM functioning is linked with depression (e.g. Demeyer et al., 2012), a significant question is whether a high WMC may *protect* against a depressed mood. Experimental studies showed that individuals with a high WMC are better able to suppress and cope with (negative) intrusions compared to their low WMC counterparts (Unsworth & Engle, 2007). Loading the WM of those people low in WMC resulted in even more difficulty with this task (Barrett, Tugade, & Engle, 2004), which can result in less suppression of

depressive cognitions (Wenzlaff & Bates, 1998). In chapter 2 we explored whether a low WMC in combination with a high WM load would indeed result in a more depressed mood. We exposed psychology students with a low and high WMC randomly to a low or high WM load *and* a sad mood induction. We hypothesized that this manipulation would result in a more depressed mood, a stronger negative bias, and more difficulty with recalling specific memories in participants with a low WMC and a high WM load compared to the other three conditions. Against expectations, we did not find that the combination of a low WMC and a high load resulted in different results than the other three conditions. However, a high WM load – independent of WMC – resulted in a larger increase of anxiety and reduction of cheerfulness compared with a low load. These results are contrary to the majority of studies, which show that people with a low WMC have more difficulties inhibiting negative thoughts (Unsworth & Engle, 2007) and thus would experience more depressed feelings, interpret ambiguous scenarios more negatively, and recall less specific autobiographical memories. This study suggests that the level of WMC is not essential for one's mood and related behavior. Some studies also found only minor (Grant, Thase, & Sweeney, 2001) or no differences (Barch, Sheline, Csernansky, & Snyder, 2003; Fossati, Amar, Raoux, Ergis, & Allilaire, 1999) in WMC between depressed and healthy individuals. As the majority of studies do find differences (e.g. Basten, Stelzel, & Fiebach, 2011; Bishop, 2009; Harvey et al., 2004; Joormann & Gotlib, 2008; Whitmer & Banich, 2007), and taking limitations of this study (small and highly educated sample, use of mood induction instead of a real depressed mood, see chapter 2) into account, future research is recommendable in exploring the role of WMC in depression.

Working memory training effect on WMC

The main aim of this dissertation was to explore the efficacy of increasing WMC on psychopathology, cognitive performance, and well-being. Empirical research shows WMC can be improved by training this memory component (e.g. Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Thorell, Lindqvist, Nutley, Bohlin, & Klingberg, 2009). The promising findings of a reduction of, for instance, ADHD symptoms (e.g. Klingberg, Forssberg, & Westerberg, 2002), schizophrenia symptoms (Subramaniam et al., 2012), and cognitive problems after a stroke (Åkerlund, Esbjörnsson, Sunnerhagen, & Björkdahl, 2013; Westerberg et al., 2007) by training WM suggest that an increase of WM is necessary to find far transfer effects. In our

studies these effects are, for example, reduced symptoms of depression or craving. We hypothesized that training WM would increase WMC and by doing so, positively affects related behavior. In line with the preconditions of Shipstead, Redick, and Engle (2012) to validly measure the effect of WM training on WMC, we used WM tasks which assessed other aspects of WM than the trained tasks.

The efficacy of WM training studies described in this dissertation show mixed results. The only hypothesized increase of WMC due to WM training was found using a gamified WM training (chapter 7) and in the study focused on decreasing rumination by training WM (chapter 4). However, we did not found effects of WM on WMC in the majority of the studies (chapters 3, 5, and 6). Important to note is that the near transfer described in chapter 4, was found on only one WM task while results of the other WM task indicated participants' WMC even decreased after training their WM. Furthermore, in both studies an increased WM did not result in a reduction of depression, anxiety, and rumination. This finding is in line with another study exploring the efficacy of WM training in a subclinical sample. Owens, Koster, and Derakshan (2013) showed a gain in WMC did not result in a reduction of self-reported rumination or depression. Further, in two of the other studies of this dissertation (chapter 3 and 6) we did not find any near transfer effect of WM training at all, similar to a recent WM training effect study of Onraedt and Koster (2014). Moreover, our study investigating WM training in SUD inpatients showed that our WM training resulted in a decrease of WMC while placebo training lead to improvement on that WM transfer task.

Our mixed and arguably disappointing results of WM training on WMC are representative for the scientific controversy about the possibility to train WM. A meta-analysis of Melby-Lervåg and Hulme (2013), for instance, concludes WM training only results in short-term and specific training effects that do not generalize to other skills. Important to note, however, is that the authors analyzed studies in which typically developing children and adults trained their WM to improve their cognitive ability, and no meta-analyses have studied the effect of WM training in (sub)clinical samples. The often referred explanation for non-transfer of WM training is that there will only be transfer to other functions and tasks with the same underlying neural networks (Olesen, Westerberg,

& Klingberg, 2004; Dahlin, Neely, Larsson, Bäckman, & Nyberg, 2008; Dahlin, Nyberg, Bäckmann, & Neely, 2008). In our studies we used both training and transfer tasks which assessed all aspects of WM – shifting, updating and inhibition – so training and transfer tasks always partly overlapped in the required WM processes, and thus in their underlying neural networks. Even transfer WM tasks addressing the same WM processes as the trained WM tasks did not reveal a strong effect of WM training on WMC in our studies. For example, in chapter 4 participants trained their WM with the Dual N-back task and executed the Internal Shift Task (IST) to measure transfer to WM on the pre-, post- and follow-up tests. Although these tasks both require shifting and updating processes of WM, no transfer effect on the IST was found.

An interesting question concerns the factors in the studies described in this dissertation in which we found a transfer effect and those in which we did not find a transfer effect to WM. When focusing on the used tasks we see that the same training and transfer tasks were used in chapter 4 – in which we found a near transfer effect on one of the tasks – as in the study in SUD patients, in which no effect was found. This difference might also be caused by the different populations used. The only other near transfer effect on WMC was found using the gamified WM training, which might suggest a gamification of WM might lead to better near transfer. As increase of WMC might bring numerous opportunities, future research needs to further explore whether increasing WMC is possible, and which factors – like training tasks, population, duration and content of training – influence a potential effect. Anyway, in our studies the number of training sessions did not have an effect on WMC increase (chapters 5 and 7).

WM training effect on psychopathology

As WM deficits might be underlying symptoms of anxiety, depression, rumination, and substance abuse (Ambrose et al., 2001; Bolla et al., 2002; Cisler & Koster, 2010; Demeyer et al., 2012; Joormann, 2006; Jovanovski et al., 2005), we hypothesized that a WM training would reduce these symptoms by decreasing WM deficits. We measured the efficacy of training WM on anxiety, depression and rumination in anxious and depressed individuals (chapters 3 and 4) and explored the effect of a gamified WM training on these measures in dysphoric students (chapter 7). Furthermore, we investigated the effect of WM

training on substance abuse, craving, impulsivity, attention bias, depression, and anxiety in SUD inpatients (chapter 5).

Contrary to our expectations, the only effect of WM training was a decrease of anxiety in one of our studies (chapter 3). This effect was only found in individuals with a diagnosis of major depression, who were, remarkably, more anxious than the ones with an anxiety disorder. The resulting suggestion, that WM training might have the most effect in individuals with a high level of anxiety, was confirmed by the finding that a higher level of anxiety on the pre-test indeed predicted a larger reduction in anxiety (chapter 3). Remarkably, this far transfer effect was found *without* a near transfer effect on WM. Our finding of far transfer without near transfer is repeatedly found in other studies (Bickel, Yi, Landes, Hill, & Baxter, 2011; Dahlin et al., 2008; Jaeggi et al., 2008; Jaeggi et al., 2010; Li et al., 2008; Schweizer, Grahn, Hampshire, Mobbs, & Dalgleish, 2013). Melby-Lervåg and Hulme (2013) are very critical about such findings in their meta-analysis. They argue that such a pattern of results does not correspond to the theory WM training is based on, which claims improvement of WMC is essential for achieving any other effects of WM training.

Focusing on the finding that WM training has the strongest effect in high anxiety individuals, it is interesting to look at the studies of Basten and colleagues (2011) and Bishop (2009). They both showed that the level of anxiety is associated with the level of WM deficits, and thus high anxious individuals have a less well functioning WM. The combination of our results and their findings suggests it might be possible that a certain extent of anxiety, and thus a certain amount of WM deficits, is needed for an effect of WM training. This might imply WM training is the most effective in high anxious individuals. However, the majority of our other studies, with both high anxious (chapter 4) and non-clinical anxious (chapters 5, 6, and 7) participants did not show an effect on anxiety.

Unfortunately, WM training did not result in reductions of other symptoms of psychopathology either. That is, WM training had no effect on rumination (chapters 3, 4, 6, and 7), depression (chapters 3 to 7), substance use and craving for substances (chapter 5) compared to placebo training. There are only a few other studies exploring the effect of WM training on rumination, depression and anxiety. A recent study of Onraedt and Koster

(2014) showed that a WM training in high ruminators had no effect on their WMC and neither on their rumination and depression symptoms. In addition, Owens and colleagues (2013) studied dysphoric students and found no effect on self-reported depression despite WM training did increase WMC at both behavioral and neural assessments. To our knowledge, no other studies have investigated WM training in anxious individuals. In sum, as there are only a few studies examining the effect of WM training on rumination, depression, and anxiety, we can cautiously conclude that WM training might not be effective in (subclinical) depressive samples, but effective in highly anxious individuals.

Regarding the lack of effect on addiction, these results are in contrast with the study of Houben et al. (2011), who found a reduction of alcohol consumption in heavy drinkers (which is different from our clinical SUD population). Importantly, they did not measure the effect of training on WMC, and thus it is unclear whether an increased WMC was the factor resulting in a reduction of alcohol consumption. Bickel and colleagues (2011), on the other hand, did measure near transfer of WM training in SUD patients. Remarkably, they found WM training led to reduced delay discounting although WMC did not increase. Both the lack of WM transfer tasks in the study of Houben and colleagues (2011) and the finding of far transfer without an increase of WMC (Bickel et al., 2011) after training, are corresponding with the criticism of a meta-analysis (Melby-Lervåg & Hulme, 2013) and a review (Shipstead et al., 2012) analyzing WM training effects. They conclude results regarding generalization of WM training to other skills are inconsistent and question whether the observed generalization is a result of change in WMC (Melby-Lervåg & Hulme, 2013; Shipstead et al., 2012). In sum, the effects of WM training as a therapy for SUD are inconsistent. We could not find evidence for the efficacy of this therapy for this clinical population.

Working memory training effect on other measures

In addition to a near and far transfer effect of WM training, we measured whether WM training would affect factors related to WMC, depression, substance use and craving – four of our main outcome measures – as well. These related factors are attention bias (chapter 5), impulsivity (chapters 5 and 6), attentional and self-control, stress, intrusions, coping, and academic performance (chapter 6). Our hypothesis regarding these factors was

that training WM would result in an increased WMC, which in turn would lead to a reduction of psychopathology and as a result, improvement of the related factors. In the study examining the efficacy of WM training in healthy students, we expected that an increased WMC would lead to improvement of academic performance and a reduction of psychopathology. This effect of WM training on those three factors would decrease intrusions, impulsivity, and stress and an improvement of coping as they are related to each other (Baddeley, 1992; Barrett et al., 2004; Engle, 2002; Houben et al., 2011; Joormann & Gotlib, 2008; Klein & Barnes, 1994; Lyubomirsky, Kasri, & Zehm, 2003; Whitmer & Banich, 2007). Unfortunately, WM training did not affect any of these measures. The most straightforward explanation for the lack of effects is that WM training did not have any effect on both WMC and depression, craving or substance use and thus, did not result in any effects on related measures either. The absence of effect is in line with the study examining whether a high WMC would protect against a depressed mood and related substrates (chapter 2). Individuals with a high WMC were not better in coping with a depressed mood than their low WMC counterparts. Experimental research first needs to reveal whether it is possible to increase WMC at all, and if so, to what extent it can transfer to psychopathology and its substrates.

Effects of time and placebo training

A consistent finding in all our studies was the reduction of psychopathology, independent of training load (chapters 3, 4, and 7). A straightforward interpretation of these results is the frequently found natural decline of these symptoms over time (Kruijshaar et al., 2005; Ramsawh, Raffa, Edelen, Rende, & Keller, 2009; Spijker et al., 2002). Furthermore, a study of Åkerlund and colleagues (2013) also found a decline of depression symptoms, regardless of the use of an adaptive or placebo training. The reduction of substance use, craving, impulsivity, and psychopathology of SUD inpatients may be attributed to the psychological treatment they received in the clinic. The improved WMC of both groups, found on one transfer WM task, might be a consequence of this treatment as well or can be attributed to a practice effect. Another possibility is that training WM, either with a low or high load, results in a reduction of psychopathology (chapters 3, 4, and 7) and psychological well-being (chapter 2). Interestingly, although psychopathology reduced, this was not always paralleled with an increase of WMC. That is,

in some studies there was an effect of time on WMC on a part of the tasks (chapters 4, 5, and 6) whereas in two other studies WMC increased on all tasks (chapters 3 and 7). As we had not included a waiting group or passive control group, we cannot determine whether improvement on psychopathology or related measures is related to improvement of WMC.

Interestingly, in one study (chapter 5) we found an increase of WMC as a result of the placebo training compared to the experimental one. In another study (chapter 4) the placebo training even led to less decrease of WMC than the experimental training. A potential explanation might be that, although the experimental training adapted to the WMC level of the participant, the level might be too high for them, leading to demotivation and/or test anxiety which might have resulted in lower performance (Cassady & Johnson, 2002; Lens & Decruyenaere, 1991) on the post-test. This suggestion is based on the finding that the experimental group rated the level and intensity of the training as higher (chapter 4) and SUD inpatients told experimenters they experienced the training as too difficult to learn from (chapter 5). Furthermore, our study manipulating WM load in students with a high and low WMC shows that a highly loaded WM resulted in more anxiety and less cheerfulness compared to a lowly loaded WM. Future studies in SUD inpatients may take into account the fact that the WM task level should start at a very easy level.

Inconsistencies WM deficits in anxious and depressed individuals

An explanation for our failure to find clear effects of WM training, are some inconsistencies in other studies. Although the majority of studies found healthy and anxious or/and depressed individuals differ in WM functioning (e.g., Basten et al., 2011; Bishop, 2009; Harvey et al., 2004; Joormann & Gotlib, 2008; Whitmer & Banich, 2007), others find only minor (Grant et al., 2001) or no differences at all (Barch et al., 2003; Fossati et al., 1999). Our results across all studies described in this thesis were representative for this controversy. Our depressed participants (chapter 4) performed worse than a healthy and even a depressed sample of another study at one WM task (Harvey et al., 2004), whereas at another WM task our depressed and anxious samples (chapters 3 and 4) did not differ in WMC compared to a healthy sample (De Lissnyder, Koster, & De Raedt, 2012). Moreover, chapter 7 shows that dysphoric and healthy students differed significantly on depression, anxiety, and rumination, but not in their WMC. This result contradicts studies

which show that dysphoric individuals show WM dysfunctions (Goeleven, De Raedt, Baert, & Koster, 2006; Joormann, 2004).

As we found only minor effects of WM training, the question is whether the absence of WM deficits might be the cause of this lack of training effect. In other words, is WM training only effective when WMC is reduced and thus, can be increased to a large extent? Since, as far as we know, our studies were the first to study WM training in clinically depressed and anxious individuals, future studies are needed to answer this question thoroughly. Anyway, it is important to note that the majority of studies *do* find that depressed and anxious individuals suffer from WM deficits. Future research needs to reveal whether these WM deficits are specific for a particular sample of depressed and anxious individuals or whether they are general in these disorders. By demarcating the sample that profits most of WM training, the efficacy of WM training can be explored in detail.

Studied sample

When concluding about the efficacy of WM training in our studies, a close look at our sample is essential. We found that in the two studies examining the effect of WM training in depressed and anxious samples (chapters 3 and 4), our participants were on average older and more highly educated compared to depressed and anxious persons in population screenings. In addition, individuals of Dutch origin were overrepresented (De Graaf et al., 2005; De Graaf, Ten Have, & Van Dorsselaer, 2010; De Wit et al., 2008; Peyrot et al., 2013). Furthermore, a high number of participants, for example 91% in chapter 4, had been in therapy (chapters 3 and 4; Centraal Bureau voor de Statistiek, 2013; Nationaal Kompas Volksgezondheid, 2013; Penninx et al., 2011; Van 't Land, Schoemaker, & De Ruiter, 2008). Also, self-reported depression and anxiety scores show that our participants were severely depressed (chapter 3; Beck, Steer, & Brown, 1996) and anxious (chapter 4; Butler, Fennell, Robson, & Gelder, 1991; Van der Ploeg, Defares, & Spielberger, 1979). An explanation for this deviance might be that our sample was recruited by advertisements in media, such as newspapers, internet, and television, and these reach and appeal more to individuals with the described characteristics. Although these studied samples were not representative for the Dutch population, their demographic characteristics may have positively influenced the motivation of the sample. Studies analyzing drop-out from

therapy show that low-education and a young age are predictive for dropping out (Edlund et al., 2002; King & Canada, 2004; Richmond, 1992; Sonawalla et al., 2002; Thormählen et al., 2003). In addition, Sonsawalla and colleagues (2002) concluded that a high extent of psychopathology results in less drop-out. Despite we already had a high drop-out (20.36% in chapter 3 and 23.47% in chapter 4), our sample characteristics and their intrinsic motivation to participate might have protected the study from even more drop-out and might indicate our sample was motivated to complete the training. This result might suggest that WM training in a more representative sample would be even less efficient in terms of drop-out. Furthermore, the general lack of effect might not be attributed to a lack of motivation. In contrast, the low motivation observed in the SUD inpatients might explain the very high drop-out rate of 65% in this study (chapter 5). Although they were not obligated to participate in the training, a significant part of the SUD inpatients would like to take part in the study. However, a great part of these participants already quit after a couple of training sessions. It might be that this type of WM training is less suitable for this population. Alternatively, a suggestion would be that these patients can first try a certain number of sessions to see whether they are motivated to enroll and maintain in the WM training. This method will save both time and money.

The fact that Houben and colleagues (2013) recruited their sample by internet and they were hazardous drinkers, while our sample consisted of detoxified SUD inpatients might partly explain the difference in WM training efficacy between these studies. The absence of substance related stimuli in the clinic might have decreased the experience of craving (Franken & Van den Brink, 2009; Franken, 2003). This floor effect may explain the lack of effect of WM training on craving and attention bias (Cox, Fadardi, & Pothos, 2006). In the studies described in chapters 2, 6, and 7, participants were psychology students. This might have undermined the manipulation in chapter 2, since the WMC of students will not differ much. Furthermore, in the gamified WM training the fact that the students were dysphoric and not depressed might have influenced the effect of this training. That is, the level of depression is related to the extent of WM deficits (e.g. Harvey et al., 2004, Joormann & Gotlib, 2008; Whitmer & Banich, 2007), and thus their level of WM deficits might have been too mild to increase with a WM training.

Pre-conditions for a WM training

One of the major issues with concluding about the efficacy of WM training is that there are numerous factors that might have an influence, like training tasks, training duration, place of training, and support during training. Moreover, these factors add up to elements that always influence efficacy, like sample, measures and experimenter-participant interaction. Shipstead and colleagues (2012) and Klingberg (2010) analyzed which preconditions must be taken into account when designing or choosing a WM training. We will discuss whether our studies met these criteria.

Firstly, studies have to use valid WM tasks that are not trained to measure near transfer. In all our studies we used valid (Conway et al., 2005; De Lissnyder et al., 2012; Kane et al., 2004; Unsworth, Heitz, Schrock, & Engle, 2005; Unsworth, Redick, Heitz, Broadway, & Engle, 2009), frequently used WM tasks that were not trained and thus, this dissertation met this criterion. Furthermore, in line with the recommendation of Conway and colleagues (2005), we used partial-credit unit scoring since empirical research showed this method of calculating scores is more valid than the often used all-or-nothing scoring. Moreover, in all studies, except the gamified WM training (chapter 7), we measured transfer WM effect with more than one WM task to measure all aspects of WM and to conclude thoroughly about WMC.

The second precondition points to the use of multiple overlapping measurements to validly measure the far transfer abilities of WM training. Our studies did not meet this precondition as we always used one self-reported questionnaire or task for measuring far transfer. Reasons for this decision were practical; the study required much effort and time for participants and adding extra questionnaires might increase drop-out due to time constraints and motivation problems. In fact, our measures have very good psychometric qualities and we doubt whether adding other, overlapping, measures would have changed the conclusions of our studies. Future research can add overlapping measures and ask participants to fill in/execute (a part of) these questionnaires/tasks from home to minimize their effort.

Thirdly, the authors advise to use a contact control group with a double blind randomization. In our studies we used double-blind randomization and all control groups received exactly the same procedure as the experimental group. In addition, the placebo training used the same tasks but on a lower and stable level compared to the experimental training. Our studies also met the fourth recommendation; raters have to be blind to condition assignment when using subjective measures of change. We only used subjective measures in chapters 3 to 5 and in all these studies raters were blind to condition. Moreover, different raters interviewed participants at the different measurements to prevent any influence of the experimenter on scores.

Regarding the fifth pre-condition, Klingberg (2010) concluded the effect of WM training is the most effective when individuals train for at least 3 weeks or 8 hours. In chapter 6 students only had to train five times 15 minutes (training component 1) and six times 25 minutes (training component 2) in a week, summing up to respectively 1 hour and 15 minutes and 2.5 hours. This is clearly a factor that might have resulted in a lack of effect on WMC and far transfer measures. However, in chapters 4 and 5, participants trained 25 minutes each of the 24 sessions, which is a total of 10 hours, but no effect on any of the measures was found. Chapters 3 and 7 have training times between this range, and no effect was found either. Furthermore, results show that the number of sessions did not predict the near transfer effect on WMC (chapters 5 and 7) or far transfer effect on craving (chapter 5) and psychopathology (chapter 7). The finding that the lack of effect was consistent despite the variety in number of training sessions and total training time, and that the number of completed training sessions had no influence on results might indicate that a too short training time might not explain our null results.

The last precondition concerns the adaptivity of the WM training to the level of the participant (Li et al., 2008; Schmiedek, Lovden, & Lindenberger, 2010). This criterion is essential as easy WM tasks lead to even more rumination (Takeuchi, Taki, & Kawashima, 2010) whereas loading WM in depressed patients resulted in better performance (Foulds, 1952). All our studies, except chapter 3, used an adaptive training for the experimental group. The study described in chapter 3, however, loaded the WM of participants as well. In sum, we can conclude that the general lack of effect of WM cannot be attributed to failures

in design or measurement. An interesting study of Redick and colleagues (2013) took all the preconditions into account and explored whether a group of young adults who executed a WM training increased on multiple measures of fluid intelligence, multitasking, WMC, crystallized intelligence, and perceptual speed compared to a no-contact control group and an active placebo-control group. Unless practice effects and a high level of statistical power, WM training did not lead to transfer on any of the cognitive abilities. Thus, even with an optimal design, no effect of WM training on WMC and related cognitive measures was found.

Methodological issues

The strength of this dissertation is that we found considerable consistent results in studies using different WM training tasks, training duration, far transfer measures and samples. However, we need to mention some limitations of our studies for a thorough interpretation of results. As we discussed specific limitations in each individual chapter, we address the caveats which are attributable to this dissertation in general. Firstly, due to large drop-out some samples are small and thus result in low power of results. The populations we used might explain this high drop-out rate partly. That is, individuals with depression, anxiety, and addiction symptoms have higher drop-out rates from treatments than populations that are used in other WM training studies, like children suffering from ADHD, healthy individuals or students with learning difficulties (e.g. Alloway, Bibile, & Lau, 2013; Jaeggi et al., 2008; Klingberg et al., 2005; Prins, Dovis, Ponsioen, Ten Brink, & Van der Oord, 2011; Siegle, Ghinassi, & Thase, 2007).

Another limitation concerns the fact that our samples in chapters 3, 4, 5, and 7, used a wide variety of medication. The experimental and placebo group did only differ in their use in the study described in chapter 4. As this concerned anti-depressants, which does not influence cognitive functioning (Harvey et al., 2004; Porter, Gallagher, Thompson, & Young, 2003), this difference probably did not influence results. Despite we found comparable medication use in the groups in other studies, we did not compare the groups on all different kinds of medication. It is possible that groups differed on this factor, which might have influenced effects of WM training. The third and fourth limitations have already been discussed extensively in this chapter and concern the non-representative samples and

the short training duration in a part of the studies (see chapter 3, 4, 6 and 7). Thus, when interpreting the results of this dissertation it is important to take these limitations into account.

Clinical implications

The clinical aim of this dissertation was to provide more insight in the efficacy of WM training for psychopathology. Unfortunately, we need to conclude that we found no evidence that WM training - given our design and measurements reduced depression, rumination, stress, intrusions, craving, substance abuse, and related measures. Advantages of computer treatments are very prominent, as this kind of therapy is cost-effective (e.g. Kaltenthaler et al., 2006; McCrone et al., 2004; Proudfoot, 2004), efficient in time (e.g. Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Kaltenthaler et al., 2006; Proudfoot, 2004), and offers a lot of possibilities, such as personal feedback and adaptation to one's WMC level and client preferences. Melby-Lervåg and Hulme (2013) express strong doubts about the clinical relevance as well as the utility of cognitive training programs in their meta-analysis. We hope this dissertation evokes the critical approach practitioners should have in evaluating and eventually, choosing therapies for their patients.

Our studies had a high drop-out rate, which would probably result in negative cost-effectiveness when operating this training program in clinical practice. For example, our drop-out rate in SUD inpatients was high (65%), even despite the presence of experimenters in the clinic, which might have increased compliance. Based on these observations we think studying the efficacy of WM training in SUD outpatients would be very difficult. Due to the low compliance rate we doubt whether WM training will be worth the effort and money invested.

Future challenges and recommendations

As a lot of factors concerning WM training might influence WM training efficacy, it might be useful to investigate these factors. The factors include the timeline of training and assessments (e.g., length of training sessions, overall duration of training period, number of assessment sessions), conditions of assessment (e.g., comfort and location of assessment, encouragement level by lab staff) as well as the setting of training (e.g., laboratory, school,

home). Regarding the design in our used WM trainings, participants frequently complained about boredom in the studies described in chapters 3 to 6. Prins and colleagues (2011) found that game elements positively influence motivation and performance during training and resulted in a better WM in children with ADHD. This study and our own observations were reasons for us to implement game elements in the WM training for dysphoric students (chapter 7). This study resulted indeed in better compliance, motivation and, most importantly, an increased WMC as compared to the other studies. Although we did not include a direct comparison. Thus, future studies investigating WM efficacy could use gamified WM studies. Another remark of participants after executing the training was that they had difficulties in linking the experienced effects of training to their daily symptoms, like depressive feelings. In our studies we encouraged them to transfer their feelings during the training – such as, feeling in control – into their daily life. For instance, when they were experiencing depressive thoughts or when they were confronted with substance related cues. A gamified training can implement such advice in a personalized way, since in our opinion this might reduce drop-out and maximize the effect of WM training.

Future research study the effects of WM training as an additional treatment, for example as addition to cognitive behavioral therapy. In two ongoing studies (not described in this dissertation) in which we combined WM training with psychological therapy, we observed that a major part of patients did not want to participate as they just started therapy and were anxious they could not combine the therapies in terms of (mental) effort. We would advise to start the WM training after one third of the therapy, at a point in time when patients are used to the therapy and therapist. They then have more capacity left to fully participate in the WM training.

Lastly, we observed that the major cause for drop-out was a lack of motivation. In our studies we rewarded participants with positive feedback and in the addiction study with a coupon of 7.50 euros. A method to increase motivation and to prevent drop-out in SUD participants might be spacing of reward, like after each completed training session. As a matter of fact, Van Gageldonk, Rigter, Ketelaars, and Van Laar (2005) conclude in their review that rewarding desired behavior is one of the most effective methods to motivate substance abusers. However, anxious and especially depressed individuals are less sensitive

for rewards (Henriques & Davidson, 2000; Tavares, Drevets, & Sahakian, 2003). In these samples reminders by telephone and email, and a case manager monitoring the progress of the patient and who can be reached by the patient, resulted in higher rates of adherence (Robertson, Smith, Castle, & Tannenbaum, 2006). We employed this method, with the experimenter in the role of case manager, but the drop-out was still high. In a combination of a computerized therapy and live sessions, it might help to reduce drop-out when the therapist occupies the role of case manager to maximize the effect of the combination of therapies.

Main conclusions

The current dissertation examined whether it is possible to reduce the negative consequences of WM deficits by increasing one's WMC. The described studies result in several valuable conclusions for both scientists and scientist practitioners. Obviously, our conclusions are based on the measurements and samples used in these studies and may not be generalizable to other measurements as well as samples. Against our hypothesis, the effect of WM training on WMC was inconsistent. However, WM training reduced anxiety in highly anxious participants and a higher level of anxiety at the start of the WM training predicted a larger reduction of anxiety due to training WM in anxious and depressed individuals. Unexpected, training WM did not result in a decrease of rumination and depression. In SUD inpatients WM training did neither result in a reduction of substance abuse, craving, attention bias for substance related items, impulsivity, depression, and anxiety. WM training in healthy students did neither lead to an increase of academic performance, coping, attentional and self-control and a reduction of stress, impulsivity, anxiety, depression, rumination, and intrusions. This last result is in line with our finding that WMC seems not to have an effect on coping with a negative mood in a healthy sample.

Increasing someone's WMC with a training and by doing so, improving his or her behavior sounds very promising and might result in numerous possibilities. However, this dissertation hopefully appeals to carefully interpret results of WM effect studies and to thoroughly explore efficacy of such trainings before exposing clinical samples to this type of treatment.

Chap-pter	Sample	Training	Training tasks	WM transfer tasks	Interaction effect	Time effect	Far transfer measures	Interaction effect	Time effect
3	105 participants with a current depressive episode	12 times during 4 weeks, 25 minutes per session	Number-letter task Updating task	IST	No	Improvement of emotional shift costs	BDI-II	No	Improvement
				SS	No	Improvement	STAI	Larger improvement in experimental group from post to FU on trait and total scales	Improvement on all STAI scales
							RRS	No	Improvement
3	62 participants with an anxiety disorder diagnosis	Idem	Idem	IST	No	Improvement of global and emotional shift costs	STAI	No	Improvement on all STAI scales
				SS	No	Improvement			
4	75 participants with a current depressive episode or anxiety disorder diagnosis	24 times during 4 weeks, 25 minutes per session	Dual N-back task SS	IST	No	Improvement of global and emotional shift costs	RRS	No	Improvement
				DS	Experimental group deteriorates	Improvement on forward score, deterioration on backward score	BDI-II	No	Improvement
				RS	Experimental group improves	No	STAI	No	Improvement on all STAI scales
5	63 participants with a SUD diagnosis	Idem	Idem	DS	No	Improvement on three of four subscales	ASI	No	Improvement on all variables

				RS	Experimental group deteriorated, placebo group improved	No	DDQ/DAQ	No	No
							OCDUS/OCDS	No	Improvement on both scales
							BIS-11	No	Improvement
							BDI-II	No	Yes
							STAI	No	Improvement on STAI trait and total
							Stroop	No	No
6	120 psychology students	Component 1: 5 days 15 minutes, component 2: 6 days 25 minutes	Component 1: RS Component 2 Dual n-back task SS	DS	No	No	VAS	No	Less sad and anxious, more cheerful and relaxed
				OS	No	Improvement on letters, deterioration on math part	BDI-II	No	Improvement
							STAI	No	Improvement on all scales
							TMAS	No	Deterioration
							RRS	No	Improvement
							IES	No	Improvement
							UCL	Deterioration of the experimental group on one scale	Improvement on four scales
							PSQ	No	Improvement
							ACS	No	Improvement
							BIS-11	No	Deterioration
							BSCS	No	Improved

	Sample	Training	Training tasks	WM transfer tasks	Interaction effect	Time effect	Far transfer measures	Interaction effect	Time effect
							Academic performance	No	Not analyzed
7	48 dysphoric students	9 sessions during 3 weeks, 30 minutes per session	Simon task SS OS Number recall task Figure task	Spanboard task	Improvement of experimental group	Improvement	BDI-II	No	Improvement
							STAI	No	Improvement on all scales
							RRS	No	No

Note: FU = Follow-up; IST = Internal Shift Task; SS = Symmetry Span; DS = Digit Span; RS = Reading Span; OS = Operation Span; BDI-II = Beck Depression Inventory Second Edition; STAI = The State-Trait Anxiety Inventory; RRS = Ruminative Response Scale; DDQ = Desires for Drug Questionnaire; DAQ = Desires for Alcohol Questionnaire; OCDUS = Obsessive Compulsive Drug Use Scale; OCDS = Obsessive Compulsive Drinking Scale; BIS-11 = Barratt Impulsivity Scale-11; BSCS = Brief Self-Control Scale; VAS = Visual Analogue Scale; TMAS = Taylor Manifest Anxiety Scale; IES = Impact of Event Scale; UCL = Utrechtse Coping Lijst; PSQ = Perceived Stress Questionnaire; ACS = Attentional Control Scale

Figure 1. Summary of working memory training designs and effects on working memory capacity, psychopathology and other measures

References

Aharonovich, E., Hasin, D. S., Brooks, A. C., Liu, X., Bisaga, A., & Nunes, E. V. (2006). Cognitive deficits predict low treatment retention in cocaine dependent patients. *Drug and Alcohol Dependence, 81*(3), 313-322.

Aiken, L. S., & West, S. G. (1990). Invalidity of true experiments self-report pretest biases. *Evaluation Review, 14*(4), 374-390.

Åkerlund, E., Esbjörnsson, E., Sunnerhagen, K. S., & Björkdahl, A. (2013). Can computerized working memory training improve impaired working memory, cognition and psychological health? *Brain Injury, 27*(13-14), 1649-1657.

Allen, D. N., Goldstein, G., & Seaton, B. E. (1997). Cognitive rehabilitation of chronic alcohol abusers. *Neuropsychology Review, 7*(1), 21-39.

Alloway, T. P., & Alloway, R. G. (2010). Investigating the predictive roles of working memory and IQ in academic attainment. *Journal of Experimental Child Psychology, 106*(1), 20-29.

Alloway, T. P., Bibile, V., & Lau, G. (2013). Computerized working memory training: Can it lead to gains in cognitive skills in students? *Computers in Human Behavior, 29*(3), 632-638.

Alterman, A. I., McDermott, P. A., Cook, T. G., Cacciola, J. S., McKay, J. R., McLellan, A. T., & Rutherford, M. J. (2000). Generalizability of the clinical dimensions of the Addiction Severity Index to nonopioid-dependent patients. *Psychology of Addictive Behaviors, 14*(3), 287.

Amado-Boccara, I., Gougoulis, N., Poirier Littre, M., Galinowski, A., & Loo, H. (1995). Effects of antidepressants on cognitive functions: A review. *Neuroscience & Biobehavioral Reviews, 19*(3), 479-493. doi:http://dx.doi.org/10.1016/0149-7634(94)00068-C

Ambrose, M. L., Bowden, S. C., & Whelan, G. (2001). Working memory impairments in alcohol-dependent participants without clinical amnesia. *Alcoholism: Clinical and Experimental Research, 25*(2), 185-191.

American Psychiatric Association. (2000). *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)*. Washington, DC: American Psychiatric Association.

Amir, N., Beard, C., & Bower, E. (2005). Interpretation bias and social anxiety. *Cognitive Therapy and Research, 29*(4), 433-443.

Anderson, M. C. (2003). Rethinking interference theory: Executive control and the mechanisms of forgetting. *Journal of Memory and Language, 49*(4), 415-445. doi:http://dx.doi.org/10.1016/j.jml.2003.08.006

Anderson, M. C., & Green, C. (2001). Suppressing unwanted memories by executive control. *Nature, 410*, 366-369.

Anderson, M. C., & Spellman, B. A. (1995). On the status of inhibitory mechanisms in cognition: Memory retrieval as a model case. *Psychological Review, 102*(1), 68.

Andrews, G., Cuijpers, P., Craske, M. G., McEvoy, P., & Titov, N. (2010). Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: A meta-analysis. *PloS One, 5*(10), e13196.

Anton, R. F., Moak, D. H., & Latham, P. (1995). The Obsessive Compulsive Drinking Scale: A self-rated instrument for the quantification of thoughts about alcohol and drinking behavior. *Alcoholism: Clinical and Experimental Research, 19*(1), 92-99.

Appleby, L., Dyson, V., Altman, E., & Luchins, D. J. (1997). Assessing substance use in multiproblem patients: Reliability and validity of the Addiction Severity Index in a mental hospital population. *The Journal of Nervous and Mental Disease, 185*(3), 159-165.

Arrindell, W., & van Rooijen, L. (1999). De VROPSOM: De meting van depressief affect met de Nederlandse bewerking van de Depression Adjective Check Lists (DACL). *Gedragstherapie, 32*, 297-304.

Bäckman, L., Nyberg, L., Soveri, A., Johansson, J., Andersson, M., Dahlin, E., . . . Rinne, J. O. (2011). Effects of working-memory training on striatal dopamine release. *Science, 333*(6043), 718. doi:10.1126/science.1204978; 10.1126/science.1204978

Baddeley, A. D. (1986). *Working memory*. New York, NY: Oxford University Press.

Baddeley, A. D., & Hitch, G. J. (1974). Working memory. *The Psychology of Learning and Motivation, 8*, 47-89.

Baddeley, A. (1992). Working memory. *Science, 255*(5044), 556-559.

Baldwin, D. S., Anderson, I. M., Nutt, D. J., Bandelow, B., Bond, A., Davidson, J. R., . . . Wittchen, H. U. (2005). Evidence-based guidelines for the pharmacological treatment of anxiety disorders: Recommendations from the British association for psychopharmacology. *Journal of Psychopharmacology, 19*(6), 567-596. doi:10.1177/0269881105059253

Baljon, M. (2007). Lichaamsgerichte interventies in de experiëntiële behandeling van angststoornissen. *Tijdschrift Voor Psychotherapie, 33*(4), 161-170.

Barch, D. M., Sheline, Y. I., Csernansky, J. G., & Snyder, A. Z. (2003). Working memory and prefrontal cortex dysfunction: Specificity to schizophrenia compared with major depression. *Biological Psychiatry, 53*(5), 376-384.

Bar-Haim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M. J., & van Ijzendoorn, M. H. (2007). Threat-related attentional bias in anxious and nonanxious individuals: A meta-analytic study. *Psychological Bulletin, 133*(1), 1.

Barrett, L. F., Tugade, M. M., & Engle, R. W. (2004). Individual differences in working memory capacity and dual-process theories of the mind. *Psychological Bulletin, 130*(4), 553.

Barth, J., Schumacher, M., & Herrmann-Lingen, C. (2004). Depression as a risk factor for mortality in patients with coronary heart disease: A meta-analysis. *Psychosomatic Medicine, 66*(6), 802-813.

Basak, C., Boot, W. R., Voss, M. W., & Kramer, A. F. (2008). Can training in a real-time strategy video game attenuate cognitive decline in older adults? *Psychology and Aging, 23*(4), 765.

Basten, U., Stelzel, C., & Fiebach, C. J. (2011). Trait anxiety modulates the neural efficiency of inhibitory control. *Journal of Cognitive Neuroscience, 23*(10), 3132-3145.

Batalla, A., Bhattacharyya, S., Yücel, M., Fusar-Poli, P., Crippa, J. A., Nogué, S., . . . Martin-Santos, R. (2013). Structural and functional imaging studies in chronic cannabis users: A systematic review of adolescent and adult findings. *PloS One, 8*(2), e55821.

Bates, M. E., Bowden, S. C., & Barry, D. (2002). Neurocognitive impairment associated with alcohol use disorders: Implications for treatment. *Experimental and Clinical Psychopharmacology, 10*(3), 193.

Beats, B., Sahakian, B. J., & Levy, R. (1996). Cognitive performance in tests sensitive to frontal lobe dysfunction in the elderly depressed. *Psychological Medicine, 26*(3), 591-604.

Bechara, A., & Martin, E. M. (2004). Impaired decision making related to working memory deficits in individuals with substance addictions. *Neuropsychology, 18*(1), 152.

Beck, A., Steer, R., & Brown, G. (1996). *Manual for the BDI-II*. San Antonio, TX: Psychological Corporation.

Bellander, M., Brehmer, Y., Westerberg, H., Karlsson, S., Fürth, D., Bergman, O., . . . Bäckman, L. (2011). Preliminary evidence that allelic variation in the LMX1A gene influences training-related working memory improvement. *Neuropsychologia, 49*(7), 1938-1942.

Bench, C. J., Friston, K. J., Brown, R. G., Scott, L. C., Frackowiak, R., & Dolan, R. J. (1992). The anatomy of melancholia - focal abnormalities of cerebral blood flow in major depression. *Psychological Medicine, 22*(3), 607-615. doi:http://dx.doi.org/10.1017/S003329170003806X

Bench, C. J., Friston, K., Brown, R., Frackowiak, R., & Dolan, R. (1993). Regional cerebral blood flow in depression measured by positron emission tomography: The relationship with clinical dimensions. *Psychological Medicine, 23*, 579-579.

Beretvas, S. N., Meyers, J. L., & Leite, W. L. (2002). A reliability generalization study of the Marlowe-Crowne Social Desirability Scale. *Educational and Psychological Measurement, 62*(4), 570-589.

Bergman Nutley, S., Söderqvist, S., Bryde, S., Thorell, L. B., Humphreys, K., & Klingberg, T. (2011). Gains in fluid intelligence after training non-verbal reasoning in 4-year-old children: A controlled, randomized study. *Developmental Science, 14*(3), 591-601.

Bickel, W. K., Yi, R., Landes, R. D., Hill, P. F., & Baxter, C. (2011). Remember the future: Working memory training decreases delay discounting among stimulant addicts. *Biological Psychiatry, 69*(3), 260-265.

Bieling, P. J., Antony, M. M., & Swinson, R. P. (1998). The State-Trait Anxiety Inventory, trait version: Structure and content re-examined. *Behaviour Research and Therapy, 36*(7-8), 777-788.

Birrer, E., Michael, T., & Munsch, S. (2007). Intrusive images in PTSD and in traumatised and non-traumatised depressed patients: A cross-sectional clinical study. *Behaviour Research and Therapy, 45*(9), 2053-2065.

Bishop, S. J. (2009). Trait anxiety and impoverished prefrontal control of attention. *Nature Neuroscience, 12*(1), 92-98.

Bjorklund, D. F., & Harnishfeger, K. K. (1990). The resources construct in cognitive development: Diverse sources of evidence and a theory of inefficient inhibition. *Developmental Review, 10*(1), 48-71.

Blaney, P. H. (1986). Affect and memory: A review. *Psychological Bulletin, 99*(2), 229.

Bobova, L., Finn, P. R., Rickert, M. E., & Lucas, J. (2009). Disinhibitory psychopathology and delay discounting in alcohol dependence: Personality and cognitive correlates. *Experimental and Clinical Psychopharmacology, 17*(1), 51.

Bolla, K. I., Brown, K., Eldreth, D., Tate, K., & Cadet, J. L. (2002). Dose-related neurocognitive effects of marijuana use. *Neurology, 59*(9), 1337-1343.

Bomyea, J., & Amir, N. (2011). The effect of an executive functioning training program on working memory capacity and intrusive thoughts. *Cognitive Therapy and Research, 35*(6), 529-535.

Borella, E., Carretti, B., Riboldi, F., & De Beni, R. (2010). Working memory training in older adults: Evidence of transfer and maintenance effects. *Psychology and Aging, 25*(4), 767.

Borkovec, T., Robinson, E., Pruzinsky, T., & DePree, J. A. (1983). Preliminary exploration of worry: Some characteristics and processes. *Behaviour Research and Therapy, 21*(1), 9-16.

Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: An update. *Trends in Cognitive Sciences, 8*(12), 539-546.

Brand, N., & Jolles, J. (1987). Information processing in depression and anxiety. *Psychological Medicine, 17*(1), 145-153.

Brandt, J., Butters, N., Ryan, C., & Bayog, R. (1983). Cognitive loss and recovery in long-term alcohol abusers. *Archives of General Psychiatry, 40*(4), 435-442.

Brewin, C. R., & Smart, L. (2005). Working memory capacity and suppression of intrusive thoughts. *Journal of Behavior Therapy and Experimental Psychiatry, 36*(1), 61-68.

Brittlebank, A. D., Scott, J., Williams, J. M., & Ferrier, I. N. (1993). Autobiographical memory in depression: State or trait marker? *The British Journal of Psychiatry, 162*, 118-121.

Broadway, J. M., & Engle, R. W. (2010). Validating running memory span: Measurement of working memory capacity and links with fluid intelligence. *Behavior Research Methods, 42*(2), 563-570.

Brom, D., & Kleber, R. J. (1985). De Schok Verwerkings Lijst [the Dutch version of the Impact of Event Scale]. *Nederlands Tijdschrift Voor De Psychologie, 40*, 164-168.

Bruce, S. E., Yonkers, K. A., Otto, M. W., Eisen, J. L., Weisberg, R. B., Pagano, M., . . . Keller, M. B. (2005). Influence of psychiatric comorbidity on recovery and recurrence in generalized anxiety disorder, social phobia, and panic disorder: A 12-year prospective study. *American Journal of Psychiatry, 162*(6), 1179-1187.

Buchwald, A. M., Strack, S., & Coyne, J. C. (1981). Demand characteristics and the Velten mood induction procedure. *Journal of Consulting and Clinical Psychology, 49*(3), 478.

Buonomano, D. V., & Merzenich, M. M. (1998). Cortical plasticity: From synapses to maps. *Annual Review of Neuroscience, 21*(1), 149-186.

Burt, D. B., Zembar, M. J., & Niederehe, G. (1995). Depression and memory impairment: A meta-analysis of the association, its pattern, and specificity. *Psychological Bulletin, 117*(2), 285.

Butler, A. C., Chapman, J. E., Forman, E. M., & Beck, A. T. (2006). The empirical status of cognitive-behavioral therapy: A review of meta-analyses. *Clinical Psychology Review, 26*(1), 17-31.

Butler, G., Fennell, M., Robson, P., & Gelder, M. (1991). Comparison of behavior therapy and cognitive behavior therapy in the treatment of generalized anxiety disorder. *Journal of Consulting and Clinical Psychology, 59*(1), 167.

Bystritsky, A. (2006). Treatment-resistant anxiety disorders. *Molecular Psychiatry, 11*(9), 805-814.

Calvo, M. G., & Ramos, P. M. (1989). Effects of test anxiety on motor learning: The processing efficiency hypothesis. *Anxiety Research, 2*(1), 45-55.

Cassady, J. C., & Johnson, R. E. (2002). Cognitive test anxiety and academic performance. *Contemporary Educational Psychology, 27*(2), 270-295.

Centraal Bureau voor de Statistiek. Opleidingsniveau van de Nederlandse bevolking. Retrieved, 2013, from http://www.trendsinbeeld.minocw.nl/grafieken/3_1_2_31.php

Channon, S., Baker, J. E., & Robertson, M. M. (1993). Working memory in clinical depression: An experimental study. *Psychological Medicine, 23*, 87-87.

Chapman, L. J., & Chapman, J. P. (1973). Problems in the measurement of cognitive deficits. *Psychological Bulletin, 79*(6), 380.

Chapman, L. J., & Chapman, J. P. (1978). The measurement of differential deficit. *Journal of Psychiatric Research, 14*, 303-311.

Chein, J. M., & Morrison, A. B. (2010). Expanding the mind's workspace: Training and transfer effects with a complex working memory span task. *Psychonomic Bulletin & Review, 17*(2), 193-199.

Christopher, G., & MacDonald, J. (2005). The impact of clinical depression on working memory. *Cognitive Neuropsychiatry, 10*(5), 379-399.

Cisler, J. M., & Koster, E. H. (2010). Mechanisms of attentional biases towards threat in anxiety disorders: An integrative review. *Clinical Psychology Review, 30*(2), 203-216.

Clark, D., James, N., Petry, N., Exner, A., Williams, A., & Norman, P. (1996). The development and validation of a questionnaire on cravings and urges for alcohol (submitted).

Coffey, C., Carlin, J. B., Lynskey, M., Li, N., & Patton, G. C. (2003). Adolescent precursors of cannabis dependence: Findings from the Victorian Adolescent Health Cohort Study. *The British Journal of Psychiatry: The Journal of Mental Science, 182*, 330-336.

Cohen, J. D., Perlstein, W. M., Braver, T. S., Nystrom, L. E., Noll, D. C., Jonides, J., & Smith, E. E. (1997). Temporal dynamics of brain activation during a working memory task. *Nature, 368*, 604-608. doi:http://dx.doi.org/10.1038/386604a0

Cohen, R. M., Weingartner, H., Smallberg, S. A., Pickar, D., & Murphy, D. L. (1982). Effort and cognition in depression. *Archives of General Psychiatry, 39*(5), 593-597.

Conway, A. R., & Getz, S. J. (2010). Cognitive ability: Does working memory training enhance intelligence? *Current Biology, 20*(8), R362-R364.

Conway, A. R. (1996). Individual differences in working memory capacity: More evidence for a general capacity theory. *Memory, 4*(6), 577-590.

Conway, A. R., Cowan, N., & Bunting, M. F. (2001). The cocktail party phenomenon revisited: The importance of working memory capacity. *Psychonomic Bulletin & Review, 8*(2), 331-335.

Conway, A. R., Kane, M. J., Bunting, M. F., Hambrick, D. Z., Wilhelm, O., & Engle, R. W. (2005). Working memory span tasks: A methodological review and user's guide. *Psychonomic Bulletin & Review, 12*(5), 769-786.

Conway, M., & Ross, M. (1984). Getting what you want by revising what you had. *Journal of Personality and Social Psychology, 47*(4), 738.

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience, 3*(3), 201-215.

Courtney, S. M., Ungerleider, L. G., Keil, K., & Haxby, J. V. (1997). Transient and sustained activity in a distributed neural system for human working memory. *Nature, 386*(6625), 608-611. doi:10.1038/386608a0

Cowan, N. (2001). The magical number 4 in short-term memory: A reconsideration of mental storage capacity. *Behavioral and Brain Sciences, 24*, 87-185.

Cox, W. M., Fadardi, J. S., & Pothos, E. M. (2006). The addiction-stroop test: Theoretical considerations and procedural recommendations. *Psychological Bulletin, 132*(3), 443.

Crane, N. A., Schuster, R. M., Fusar-Poli, P., & Gonzalez, R. (2013). Effects of cannabis on neurocognitive functioning: Recent advances, neurodevelopmental influences, and sex differences. *Neuropsychology Review, 23*(2), 117-137.

Crean, R. D., Crane, N. A., & Mason, B. J. (2011). An evidence based review of acute and long-term effects of cannabis use on executive cognitive functions. *Journal of Addiction Medicine, 5*(1), 1-8. doi:10.1097/ADM.0b013e31820c23fa [doi]

Crone, E. A., Wendelken, C., Donohue, S., van Leijenhorst, L., & Bunge, S. A. (2006). Neurocognitive development of the ability to manipulate information in working memory. *Proceedings of the National Academy of Sciences of the United States of America, 103*(24), 9315-9320. doi:10.1073/pnas.0510088103

Crowne, D. P., & Marlowe, D. (1960). A new scale of social desirability independent of psychopathology. *Journal of Consulting Psychology, 24*(4), 349.

Cuijpers, P. (2006). De depressieve stoornis. In J. E. Hovens, & H. J. G. M. van Megen (Eds.), *Handboek psychologische psychiatrie* (pp. 233-246). Utrecht: De Tijdstroom.

Cuijpers, P., & Dekker, J. (2005). Psychologische behandeling van depressie: Een systematisch overzicht van meta-analyses. *Nederlands Tijdschrift Voor Geneeskunde, 149*, 1892-1897.

Cuijpers, P., Smit, F., Bohlmeijer, E., Hollon, S. D., & Andersson, G. (2010). Efficacy of cognitive-behavioural therapy and other psychological treatments for adult depression: Meta-analytic study of publication bias. *The British Journal of Psychiatry, 196*(3), 173-178. doi:10.1192/bjp.bp.109.066001; 10.1192/bjp.bp.109.066001

Curtis, C. E., & D'Esposito, M. (2003). Persistent activity in the prefrontal cortex during working memory. *Trends in Cognitive Sciences, 7*(9), 415-423.

Daches, S., & Mor, N. (2013). Training ruminators to inhibit negative information: A preliminary report. *Cognitive Therapy and Research, 38*, 1-12.

Daches, S., Mor, N., Winquist, J., & Gilboa-Schechtman, E. (2010). Brooding and attentional control in processing self-encoded information: Evidence from a modified garner task. *Cognition and Emotion, 24*(5), 876-885.

Dahlin, E., Nyberg, L., Bäckman, L., & Neely, A. S. (2008). Plasticity of executive functioning in young and older adults: Immediate training gains, transfer, and long-term maintenance. *Psychology and Aging, 23*(4), 720.

Dahlin, K. I. (2011). Effects of working memory training on reading in children with special needs. *Reading and Writing, 24*(4), 479-491.

Dahlin, E., Neely, A. S., Larsson, A., Bäckman, L., & Nyberg, L. (2008). Transfer of learning after updating training mediated by the striatum. *Science, 320*(5882), 1510-1512. doi:10.1126/science.1155466; 10.1126/science.1155466

Dalgleish, T., Spinks, H., Yiend, J., & Kuyken, W. (2001). Autobiographical memory style in seasonal affective disorder and its relationship to future symptom remission. *Journal of Abnormal Psychology, 110*(2), 335.

Daneman, M., & Carpenter, P. A. (1980). Individual differences in working memory and reading. *Journal of Verbal Learning and Verbal Behavior, 19*(4), 450-466.

Darke, S. (1988). Anxiety and working memory capacity. *Cognition and Emotion, 2*(2), 145-154.

De Graaf, H., ten Have, M., van Dorsselaer, S., Schoemaker, C., Beekman, A., & Vollebergh, W. (2005). Verschillen tussen etnische groepen in psychiatrische morbiditeit. Resultaten van NEMESIS. *Maandblad Geestelijke Volksgezondheid, 60*, 703-716.

De Graaf, R., ten Have, M., & van Dorsselaer, S. (2010). *De psychische gezondheid van de Nederlandse bevolking*. Utrecht: Trimbos-Instituut.

De Graaf, R., ten Have, M., van Gool, C., & van Dorsselaer, S. (2012). Prevalence of mental disorders and trends from 1996 to 2009. Results from the Netherlands Mental Health Survey and Incidence Study-2. *Social Psychiatry and Psychiatric Epidemiology, 47*(2), 203-213.

De Lissnyder, E., Koster, E. H., & De Raedt, R. (2012). Emotional interference in working memory is related to rumination. *Cognitive Therapy and Research, 36*(4), 348-357.

De Lissnyder, E., Koster, E. H., Goubert, L., Onraedt, T., Vanderhasselt, M., & De Raedt, R. (2012). Cognitive control moderates the association between stress and rumination. *Journal of Behavior Therapy and Experimental Psychiatry, 43*(1), 519-525.

De Raedt, R., & Koster, E. H. (2010). Understanding vulnerability for depression from a cognitive neuroscience perspective: A reappraisal of attentional factors and a new conceptual framework. *Cognitive, Affective, & Behavioral Neuroscience, 10*(1), 50-70.

De Wit, H. (2009). Impulsivity as a determinant and consequence of drug use: A review of underlying processes. *Addiction Biology, 14*(1), 22-31.

De Wit, M. A., Tuinebreijer, W. C., Dekker, J., Beekman, A. T., Gorissen, W. H., Schrier, A. C., . . . Verhoeff, A. P. (2008). Depressive and anxiety disorders in different ethnic groups. *Social Psychiatry and Psychiatric Epidemiology, 43*(11), 905-912.

DeLoache, J. S., Chiong, C., Sherman, K., Islam, N., Vanderborght, M., Troseth, G. L., . . . O'Doherty, K. (2010). Do babies learn from baby media? *Psychological Science, 21*(11), 1570-1574. doi:10.1177/0956797610384145; 10.1177/0956797610384145

Demeyer, I., De Lissnyder, E., Koster, E. H., & De Raedt, R. (2012). Rumination mediates the relationship between impaired cognitive control for emotional information and depressive symptoms: A prospective study in remitted depressed adults. *Behaviour Research and Therapy, 50*(5), 292-297.

Dennis, M., & Scott, C. K. (2007). Managing addiction as a chronic condition. *Addiction Science & Clinical Practice, 4*(1), 45-55.

Denny, E. B., & Hunt, R. R. (1992). Affective valence and memory in depression: Dissociation of recall and fragment completion. *Journal of Abnormal Psychology, 101*(3), 575.

Deroma, V. M., Leach, J. B., & Leverett, J. P. (2009). The relationship between depression and college academic performance. *College Student Journal, 43*(2), 325-334.

Derryberry, D., & Reed, M. A. (2002). Anxiety-related attentional biases and their regulation by attentional control. *Journal of Abnormal Psychology, 111*(2), 225.

D'Esposito, M., Detre, J. A., Alsop, D. C., Shin, R. K., Atlas, S., & Grossman, M. (1995). The neural basis of the central executive system of working memory. *Nature, 378*(6554), 279-281.

Dobbs, A. R., & Rule, B. G. (1989). Adult age differences in working memory. *Psychology and Aging, 4*(4), 500.

Dobson, K. S., & Dozois, D. J. (2001). Historical and philosophical bases of the cognitive-behavioral therapies. In K. S. Dobson (Ed.), *Handbook of cognitive-behavioral therapies* (Second ed.). New York, NY: Guilford Press.

Dodge, K., Krantz, B., Kenny, P. J., & Suciu, G. P. (2013). Substance abuse treatment modalities and outcomes in a naturalistic setting. *Addictive Disorders & their Treatment, 12*(2), 76-90.

Dolan, R. J., Bench, C. J., Brown, R. G., Scott, L. C., Friston, K. J., & Frackowiak, R. S. (1992). Regional cerebral blood flow abnormalities in depressed patients with cognitive impairment. *Journal of Neurology, Neurosurgery, and Psychiatry, 55*(9), 768-773.

Dolan, R. J., Bench, C. J., Liddle, P. F., Friston, K. J., Frith, C. D., Grasby, P. M., & Frackowiak, R. S. (1993). Dorsolateral prefrontal cortex dysfunction in the major

psychoses; symptom or disease specificity? *Journal of Neurology, Neurosurgery, and Psychiatry, 56*(12), 1290-1294.

Doris, A., Ebmeier, K., & Shajahan, P. (1999). Depressive illness. *The Lancet, 354*(9187), 1369-1375.

Dorrepaal, E., van Nieuwenhuizen, C., Schene, A., & de Haan, R. (1998). De effectiviteit van cognitieve en interpersoonlijke therapie bij depressiebehandeling: Een meta-analyse. *Tijdschrift Voor Psychiatrie, 40*(1), 27-39.

Drenth, P. J. (1965). *Test voor Niet-Verbale Abstractie*. Amsterdam: Swets & Zeitlinger.

Dretsch, M. N., & Tipples, J. (2008). Working memory involved in predicting future outcomes based on past experiences. *Brain and Cognition, 66*(1), 83-90.

Edlund, M. J., Wang, P. S., Berglund, P. A., Katz, S. J., Lin, E., & Kessler, R. C. (2002). Dropping out of mental health treatment: Patterns and predictors among epidemiological survey respondents in the United States and Ontario. *American Journal of Psychiatry, 159*(5), 845-851.

Egeland, J., Rund, B., Sundet, K., Landrø, N., Asbjørnsen, A., Lund, A., . . . Hugdahl, K. (2003). Attention profile in schizophrenia compared with depression: Differential effects of processing speed, selective attention and vigilance. *Acta Psychiatrica Scandinavica, 108*(4), 276-284.

Elderkin-Thompson, V., Kumar, A., Bilker, W. B., Dunkin, J. J., Mintz, J., Moberg, P. J., . . . Gur, R. E. (2003). Neuropsychological deficits among patients with late-onset minor and major depression. *Archives of Clinical Neuropsychology, 18*(5), 529-549.

Elliott, R., Sahakian, B. J., McKay, A. P., Herrod, J. J., Robbins, T. W., & Paykel, E. S. (1996). Neuropsychological impairments in unipolar depression: The influence if perceived failure on subsequent performance. *Psychological Medicine, 26*, 975-989.

Elliott, R., Sahakian, B., Michael, A., Paykel, E., & Dolan, R. (1998). Abnormal neural response to feedback on planning and guessing tasks in patients with unipolar depression. *Psychological Medicine, 28*(3), 559-571.

Elliott, R., Sahakian, B. J., Herrod, J. J., Robbins, T. W., & Paykel, E. S. (1997). Abnormal response to negative feedback in unipolar depression: Evidence for a diagnosis specific impairment. *Journal of Neurology, Neurosurgery, and Psychiatry, 63*(1), 74-82.

Emmelkamp, P. M. G., Bouman, T. K., & Visser, P. (2008). *Angststoornissen en hypochondrie*. Houten: Bohn Stafleu van Loghum.

Engle, R. W. (2002). Working memory capacity as executive attention. *Current Directions in Psychological Science, 11*(1), 19-23.

Engle, R. W., Kane, M. J., & Tuholski, S. W. (1999). Individual differences in working memory capacity and what they tell us about controlled attention, general fluid intelligence, and functions of the prefrontal cortex. In A. Miyake, & P. Shah (Eds.), *Mechanisms of active maintenance and executive control,* (pp. 102-134). New York, NY: Cambridge University Press.

Engle, R. W., Tuholski, S. W., Laughlin, J. E., & Conway, A. R. (1999). Working memory, short-term memory, and general fluid intelligence: A latent-variable approach. *Journal of Experimental Psychology: General, 128*(3), 309.

Enright, S. J., & Beech, A. R. (1990). Obsessional states: Anxiety disorders or schizotypes? An information processing and personality assessment. *Psychological Medicine, 20*(3), 621-627.

Evans, J., Williams, J., O'loughlin, S., & Howells, K. (1992). Autobiographical memory and problem-solving strategies of parasuicide patients. *Psychological Medicine, 22*(2), 399-405.

Evers, A., van Vliet-Mulder, J., & Groot, C. (2005). *Documentatie van tests en testresearch in Nederland, aanvulling 2005/01 (COTAN)*. Amsterdam: Boom test uitgevers.

Eysenck, M. W., & Derakshan, N. (1998). Working memory capacity in high trait-anxious and repressor groups. *Cognition & Emotion, 12*(5), 697-713.

Eysenck, M. W. (1979). Anxiety, learning, and memory: A reconceptualization. *Journal of Research in Personality, 13*(4), 363-385.

Eysenck, M. W. (1982). *Attention and arousal: Cognition and performance*. Berlin: Springer-Verlag.

Eysenck, M. W., & Calvo, M. G. (1992). Anxiety and performance: The processing efficiency theory. *Cognition & Emotion, 6*(6), 409-434.

Eysenck, M. W., Derakshan, N., Santos, R., & Calvo, M. G. (2007). Anxiety and cognitive performance: Attentional control theory. *Emotion, 7*(2), 336.

Eysenck, M. W., MacLeod, C., & Mathews, A. (1987). Cognitive functioning and anxiety. *Psychological Research, 49*(2-3), 189-195.

Falconer, E., Bryant, R., Felmingham, K. L., Kemp, A. H., Gordon, E., Peduto, A., . . . Williams, L. M. (2008). The neural networks of inhibitory control in posttraumatic stress disorder. *Journal of Psychiatry & Neuroscience, 33*(5), 413-422.

Fergusson, D. M., Poulton, R., Smith, P. F., & Boden, J. M. (2006). Cannabis and psychosis. *British Medical Journal (Clinical Research Ed.), 332*(7534), 172-175.

Field, M., & Cox, W. M. (2008). Attentional bias in addictive behaviors: A review of its development, causes, and consequences. *Drug and Alcohol Dependence, 97*(1), 1-20.

Finn, P. R., & Hall, J. (2004). Cognitive ability and risk for alcoholism: Short-term memory capacity and intelligence moderate personality risk for alcohol problems. *Journal of Abnormal Psychology, 113*(4), 569.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. (1996). *Structured Clinical Interview for DSM-IV-TR axis I disorders (SCID-I) (patient edition)*. New York, NY: Biometrics Research Department.

Fossati, P., Amar, G., Raoux, N., Ergis, A. M., & Allilaire, J. F. (1999). Executive functioning and verbal memory in young patients with unipolar depression and schizophrenia. *Psychiatry Research, 89*(3), 171-187.

Foulds, G. (1952). Temperamental differences in maze performance. *British Journal of Psychology, 43*(1), 33-41.

Franken, I., & van den Brink, W. (2009). *Handboek verslaving*. Utrecht: De Tijdstroom.

Franken, I. H. (2003). Drug craving and addiction: Integrating psychological and neuropsychopharmacological approaches. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 27*(4), 563-579.

Franken, I. H., Hendriks, V. M., & van den Brink, W. (2002). Initial validation of two opiate craving questionnaires: The Obsessive Compulsive Drug Use Scale and the Desires for Drug Questionnaire. *Addictive Behaviors, 27*(5), 675-685.

Franken, I. H., Rosso, M., & van Honk, J. (2003). Selective memory for alcohol cues in alcoholics and its relation to craving. *Cognitive Therapy and Research, 27*(4), 481-488.

Fresco, D. M., Frankel, A. N., Mennin, D. S., Turk, C. L., & Heimberg, R. G. (2002). Distinct and overlapping features of rumination and worry: The relationship of cognitive production to negative affective states. *Cognitive Therapy and Research, 26*(2), 179-188.

Friedman, N. P., & Miyake, A. (2004). The relations among inhibition and interference control functions: A latent-variable analysis. *Journal of Experimental Psychology: General, 133*(1), 101.

Frith, C. D. (1979). Consciousness, information processing and schizophrenia. *The British Journal of Psychiatry, 134*, 225-235.

Fröjd, S. A., Nissinen, E. S., Pelkonen, M. U., Marttunen, M. J., Koivisto, A., & Kaltiala-Heino, R. (2008). Depression and school performance in middle adolescent boys and girls. *Journal of Adolescence, 31*(4), 485-498.

Gendle, M. H., & Ransom, M. R. (2006). Use of the electronic game SIMON® as a measure of working memory span in college age adults. *Journal of Behavioral and Neuroscience Research, 4*, 1-7.

Geraerts, E., Merckelbach, H., Jelicic, M., & Habets, P. (2007). Suppression of intrusive thoughts and working memory capacity in repressive coping. *The American Journal of Psychology, 120*(2), 205-218.

Gloaguen, V., Cottraux, J., Cucherat, M., & Blackburn, I. (1998). A meta-analysis of the effects of cognitive therapy in depressed patients. *Journal of Affective Disorders, 49*(1), 59-72.

Goeleven, E., De Raedt, R., Baert, S., & Koster, E. H. (2006). Deficient inhibition of emotional information in depression. *Journal of Affective Disorders, 93*(1), 149-157.

Gold, J. M., Goldberg, T. E., & Weinberger, D. R. (1992). Prefrontal function and schizophrenic symptoms. *Cognitive and Behavioral Neurology, 5*(4), 253-261.

Goldstein, R. Z., & Volkow, N. D. (2002). Drug addiction and its underlying neurobiological basis: Neuroimaging evidence for the involvement of the frontal cortex. *American Journal of Psychiatry, 159*(10), 1642-1652.

Gorenstein, C., Caldeira de Carvalho, S., Artes, R., Moreno, R. A., & Marcourakis, T. (2006). Cognitive performance in depressed patients after chronic use of antidepressants. *Psychopharmacology, 185*(1), 84-92.

Gorman, J. M. (1996). Comorbid depression and anxiety spectrum disorders. *Depression and Anxiety, 4*(4), 160-168.

Gotlib, I. H., & Joormann, J. (2010). Cognition and depression: Current status and future directions. *Annual Review of Clinical Psychology, 6*, 285.

Grant, M. M., Thase, M. E., & Sweeney, J. A. (2001). Cognitive disturbance in outpatient depressed younger adults: Evidence of modest impairment. *Biological Psychiatry, 50*(1), 35-43.

Gray, J. R., Chabris, C. F., & Braver, T. S. (2003). Neural mechanisms of general fluid intelligence. *Nature Neuroscience, 6*(3), 316-322.

Greenwald, A. G., Spangenberg, E. R., Pratkanis, A. R., & Eskenazi, J. (1991). Double-blind tests of subliminal self-help audiotapes. *Psychological Science, 2*(2), 119-122.

Groenestijn, M., Akkerhuis, G., Kupka, R., Schneider, N., & Nolen, W. (1999). *Gestructureerd klinisch interview voor de vaststelling van DSM-IV as I stoornissen (SCID-I; Dutch version)*. Lisse: Swets & Zeitlinger.

Gross, J. J., & Thompson, R. A. (2007). Emotion regulation: Conceptual foundations. In J. J. Gross (Ed.), *Handbook of emotion regulation* (pp. 3-24). New York, NY: Guilford Press.

Grossman, I., Kaufman, A. S., Mednitsky, S., Scharff, L., & Dennis, B. (1994). Neurocognitive abilities for a clinically depressed sample versus a matched control group of normal individuals. *Psychiatry Research, 51*(3), 231-244.

Gunn, R. L., & Finn, P. R. (2013). Impulsivity partially mediates the association between reduced working memory capacity and alcohol problems. *Alcohol, 47*(1), 3-8.

Harvey, A. G., Bryant, R. A., & Dang, S. T. (1998). Autobiographical memory in acute stress disorder. *Journal of Consulting and Clinical Psychology, 66*(3), 500.

Harvey, P., Le Bastard, G., Pochon, J., Levy, R., Allilaire, J., Dubois, B., & Fossati, P. (2004). Executive functions and updating of the contents of working memory in unipolar depression. *Journal of Psychiatric Research, 38*(6), 567-576.

Hasher, L., Lustig, C., & Zacks, R. (2007). Inhibitory mechanisms and the control of attention. In A. Conway, C. Jarrold, M. Kane & J. Towse (Eds.), *Variation in working memory*. (pp. 227-249). New York, NY: Oxford University Press.

Hasher, L., Zacks, R. T., & May, C. P. (1999). Inhibitory control, circadian arousal, and age. In D. Gopher, & A. Koriat (Eds.), *Attention and performance XVII* (pp. 653-675). Cambridge: The MIT Press.

Hasselbalch, B. J., Knorr, U., & Kessing, L. V. (2011). Cognitive impairment in the remitted state of unipolar depressive disorder: A systematic review. *Journal of Affective Disorders, 134*(1), 20-31.

Hayes, S., Hirsch, C., & Mathews, A. (2008). Restriction of working memory capacity during worry. *Journal of Abnormal Psychology, 117*(3), 712.

Hembree, R. (1988). Correlates, causes, effects, and treatment of test anxiety. *Review of Educational Research, 58*(1), 47-77.

Hempel, A., Giesel, F. L., Caraballo, N. M. G., Amann, M., Meyer, H., Wüstenberg, T., . . . Schröder, J. (2004). Plasticity of cortical activation related to working memory during training. *American Journal of Psychiatry, 161*(4), 745-747.

Hendriks, V. M., Kaplan, C. D., van Limbeek, J., & Geerlings, P. (1989). The Addiction Severity Index: Reliability and validity in a Dutch addict population. *Journal of Substance Abuse Treatment, 6*(2), 133-141.

Henriques, J. B., & Davidson, R. J. (2000). Decreased responsiveness to reward in depression. *Cognition & Emotion, 14*(5), 711-724.

Hertel, P. (2004). Memory for emotional and nonemotional events in depression. In D. Reisberg, & P. Hertel (Eds.), *Memory and emotion* (pp. 186-216). Oxford: Oxford University Press.

Hertel, P. T. (1997). On the contributions of deficent cognitive control to memory impairments in depression. *Cognition & Emotion, 11*(5-6), 569-583.

Hertel, P. T. (1998). Relation between rumination and impaired memory in dysphoric moods. *Journal of Abnormal Psychology, 107*(1), 166.

Hester, R., & Garavan, H. (2005). Working memory and executive function: The influence of content and load on the control of attention. *Memory & Cognition, 33*(2), 221-233.

Hinson, J. M., Jameson, T. L., & Whitney, P. (2003). Impulsive decision making and working memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 29*(2), 298.

Hinson, J. M., & Whitney, P. (2006). Working memory load and decision making: A reply to franco-watkins, pashler, and rickard (2006). *Journal of Experimental Psychology: Learning, Memory, and Cognition, 32*(2), 448-450.

Hofmann, W., Gschwendner, T., Friese, M., Wiers, R. W., & Schmitt, M. (2008). Working memory capacity and self-regulatory behavior: Toward an individual differences perspective on behavior determination by automatic versus controlled processes. *Journal of Personality and Social Psychology, 95*(4), 962.

Holmes, E. A., Lang, T. J., & Shah, D. M. (2009). Developing interpretation bias modification as a" cognitive vaccine" for depressed mood: Imagining positive events makes you feel better than thinking about them verbally. *Journal of Abnormal Psychology, 118*(1), 76.

Holmes, J., Gathercole, S. E., & Dunning, D. L. (2009). Adaptive training leads to sustained enhancement of poor working memory in children. *Developmental Science, 12*(4), F9-F15. doi:10.1111/j.1467-7687.2009.00848.x

Horowitz, M., Wilner, N., & Alvarez, W. (1979). Impact of Event Scale: A measure of subjective stress. *Psychosomatic Medicine, 41*(3), 209-218.

Houben, K., Wiers, R. W., & Jansen, A. (2011). Getting a grip on drinking behavior: Training working memory to reduce alcohol abuse. *Psychological Science, 22*(7), 968-975. doi:10.1177/0956797611412392; 10.1177/0956797611412392

Howell, A., & Conway, M. (1992). Mood and the suppression of positive and negative self-referent thoughts. *Cognitive Therapy and Research, 16*(5), 535-555.

Hutschemaekers, H., Donker, M., & Rigter, H. (1999). *De geestelijke gezondheidszorg in beweging.* Trimbos Instituut.

Hysenbegasi, A., Hass, S. L., & Rowland, C. R. (2005). The impact of depression on the academic productivity of university students. *Journal of Mental Health Policy and Economics, 8*(3), 145.

Ilkowska, M., & Engle, R. W. (2010). Trait and state differences in working memory capacity. In A. Gruszka, G. Matthews & B. Szymura (Eds.), *Handbook of individual differences in cognition* (pp. 295-320). New York, NY: Springer. doi:10.1007/978-1-4419-1210-7_18

Isen, A. M. (1984). Toward understanding the role of affect in cognition. In R. S. Wyer, & T. K. Srull (Eds.), *Handbook of social cognition* (pp. 179-236). Hillsdale, NJ: Erlbaum.

Jack, A. I., Dawson, A. J., Begany, K. L., Leckie, R. L., Barry, K. P., Ciccia, A. H., & Snyder, A. Z. (2013). fMRI reveals reciprocal inhibition between social and physical cognitive domains. *Neuroimage, 66*, 385-401.

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Perrig, W. J. (2008). Improving fluid intelligence with training on working memory. *Proceedings of the National Academy of Sciences, 105*(19), 6829-6833.

Jaeggi, S. M., Studer-Luethi, B., Buschkuehl, M., Su, Y., Jonides, J., & Perrig, W. J. (2010). The relationship between n-back performance and matrix reasoning - Implications for training and transfer. *Intelligence, 38*(6), 625-635.

Jaeggi, S. M., Buschkuehl, M., Etienne, A., Ozdoba, C., Perrig, W. J., & Nirkko, A. C. (2007). On how high performers keep cool brains in situations of cognitive overload. *Cognitive, Affective and Behavioral Neuroscience, 7*(2), 75-89.

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Shah, P. (2011). Short- and long-term benefits of cognitive training. *Proceedings of the National Academy of Sciences of the United States of America, 108*(25), 10081-10086.

Jolles, D. D., Grol, M. J., Van Buchem, M. A., Rombouts, S. A., & Crone, E. A. (2010). Practice effects in the brain: Changes in cerebral activation after working memory practice depend on task demands. *Neuroimage, 52*(2), 658-668.

Jonides, J., Lewis, R. L., Nee, D. E., Lustig, C. A., Berman, M. G., & Moore, K. S. (2008). The mind and brain of short-term memory. *Annual Review of Psychology, 59*, 193-224.

Joormann, J. (2004). Attentional bias in dysphoria: The role of inhibitory processes. *Cognition and Emotion, 18*(1), 125-147.

Joormann, J. (2005). Inhibition, rumination, and mood regulation in depression. In R. W. Engle, G. Sedek, U. von Hecker & D. N. McIntosh (Eds.), *Cognitive limitations in aging and psychopathology: Attention, working memory, and executive functions* (pp. 275-312). New York, NY: Cambridge University Press.

Joormann, J. (2006). Differential effects of rumination and dysphoria on the inhibition of irrelevant emotional material: Evidence from a negative priming task. *Cognitive Therapy and Research, 30*(2), 149-160.

Joormann, J. (2010). Cognitive inhibition and emotion regulation in depression. *Current Directions in Psychological Science, 19*(3), 161-166.

Joormann, J., & Gotlib, I. H. (2007). Selective attention to emotional faces following recovery from depression. *Journal of Abnormal Psychology, 116*(1), 80.

Joormann, J., & Gotlib, I. H. (2008). Updating the contents of working memory in depression: Interference from irrelevant negative material. *Journal of Abnormal Psychology, 117*(1), 182.

Joormann, J., Hertel, P. T., LeMoult, J., & Gotlib, I. H. (2009). Training forgetting of negative material in depression. *Journal of Abnormal Psychology, 118*(1), 34.

Joormann, J., Nee, D. E., Berman, M. G., Jonides, J., & Gotlib, I. H. (2010). Interference resolution in major depression. *Cognitive, Affective, & Behavioral Neuroscience, 10*(1), 21-33.

Jovanovski, D., Erb, S., & Zakzanis, K. K. (2005). Neurocognitive deficits in cocaine users: A quantitative review of the evidence. *Journal of Clinical and Experimental Neuropsychology, 27*(2), 189-204.

Kaltenthaler, E., Brazier, J., De Nigris, E., Tumur, I., Ferriter, M., Beverley, C., . . . Sutcliffe, P. A. (2006). Computerised cognitive behaviour therapy for depression and anxiety update: A systematic review and economic evaluation. *Health Technology Assessment, 10*(33), 1-186.

Kanayama, G., Rogowska, J., Pope, H. G., Gruber, S. A., & Yurgelun-Todd, D. A. (2004). Spatial working memory in heavy cannabis users: A functional magnetic resonance imaging study. *Psychopharmacology, 176*(3-4), 239-247.

Kane, M. J., Conway, A. R., Hambrick, D. Z., & Engle, R. W. (2007). Variation in working memory capacity as variation in executive attention and control. In A. R. A. Conway, C. Jarrold, M. J. Kane, A. Miyake & J. N. Towse (Eds.), *Variation in working memory* (pp. 21-48). Oxford: Oxford University Press.

Kane, M. J., Hambrick, D. Z., Tuholski, S. W., Wilhelm, O., Payne, T. W., & Engle, R. W. (2004). The generality of working memory capacity: A latent-variable approach to verbal and visuospatial memory span and reasoning. *Journal of Experimental Psychology: General, 133*(2), 189.

Kane, M. J., & Engle, R. W. (2002). The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: An individual-differences perspective. *Psychonomic Bulletin and Review, 9*(4), 637-671.

Karbach, J., & Kray, J. (2009). How useful is executive control training? Age differences in near and far transfer of task-switching training. *Developmental Science, 12*(6), 978-990.

Keller, M. B., & Boland, R. J. (1998). Implications of failing to achieve successful long-term maintenance treatment of recurrent unipolar major depression. *Biological Psychiatry, 44*(5), 348-360.

Kerssemakers, R., van Meerten, R., Noorlander, E., & Vervaeke, H. (2008). *Drugs en alcohol: Gebruik, misbruik en verslaving*. Houten: Bohn Stafleu van Loghum.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Archives of General Psychiatry, 62*(6), 593-602.

King, A. C., & Canada, S. A. (2004). Client-related predictors of early treatment drop-out in a substance abuse clinic exclusively employing individual therapy. *Journal of Substance Abuse Treatment, 26*(3), 189-195.

King, R., & Schaefer, A. (2011). The emotional startle effect is disrupted by a concurrent working memory task. *Psychophysiology, 48*(2), 269-272.

Kirchner, W. K. (1958). Age differences in short-term retention of rapidly changing information. *Journal of Experimental Psychology, 55*(4), 352.

Klein, K., & Barnes, D. (1994). The relationship of life stress to problem solving: Task complexity and individual differences. *Social Cognition, 12*(3), 187-204.

Klein, K., & Boals, A. (2001). The relationship of life event stress and working memory capacity. *Applied Cognitive Psychology, 15*(5), 565-579.

Klingberg, T. (2010). Training and plasticity of working memory. *Trends in Cognitive Sciences, 14*(7), 317-324.

Klingberg, T., Fernell, E., Olesen, P. J., Johnson, M., Gustafsson, P., Dahlström, K., . . . Westerberg, H. (2005). Computerized training of working memory in children with ADHD - a randomized, controlled trial. *Journal of the American Academy of Child & Adolescent Psychiatry, 44*(2), 177-186.

Klingberg, T., Forssberg, H., & Westerberg, H. (2002). Training of working memory in children with ADHD. *Journal of Clinical and Experimental Neuropsychology, 24*(6), 781-791.

Klingberg, T., Kawashima, R., & Roland, P. E. (1996). Activation of multi-modal cortical areas underlies short-term memory. *European Journal of Neuroscience, 8*(9), 1965-1971.

Knol, M., Twisk, J., Beekman, A., Heine, R., Snoek, F., & Pouwer, F. (2006). Depression as a risk factor for the onset of type 2 diabetes mellitus. A meta-analysis. *Diabetologia, 49*(5), 837-845.

Koster, E. H., De Lissnyder, E., & De Raedt, R. (2013). Rumination is characterized by valence-specific impairments in switching of attention. *Acta Psychologica, 144*(3), 563-570.

Koster, E. H., Soetens, B., Braet, C., & De Raedt, R. (2008). How to control a white bear? Individual differences involved in self-perceived and actual thought-suppression ability. *Cognition and Emotion, 22*(6), 1068-1080.

Kraanen, F., Emmelkamp, P., & de Wildt, W. (2007). Psychopathologie bij behandelde verslaafden: Een onderzoek naar comorbiditeit. *Verslaving, 3*(4), 3-13.

Krames, L., & MacDonald, M. (1985). Distraction and depressive cognitions. *Cognitive Therapy and Research, 9*(5), 561-573.

Kruijshaar, M. E., Barendregt, J., Vos, T., de Graaf, R., Spijker, J., & Andrews, G. (2005). Lifetime prevalence estimates of major depression: An indirect estimation method and a quantification of recall bias. *European Journal of Epidemiology, 20*(1), 103-111.

Kuijer, R., de Ridder, D., Ouwehand, C., Houx, B., & van den Bos, R. (2008). Dieting as a case of behavioural decision making. Does self-control matter? *Appetite, 51*(3), 506-511.

Kuyken, W., & Dalgleish, T. (2011). Overgeneral autobiographical memory in adolescents at risk for depression. *Memory, 19*(3), 241-250.

Kwon, H., Reiss, A. L., & Menon, V. (2002). Neural basis of protracted developmental changes in visuo-spatial working memory. *Proceedings of the National Academy of Sciences of the United States of America, 99*(20), 13336-13341. doi:10.1073/pnas.162486399

Lawson, C., & MacLeod, C. (1999). Depression and the interpretation of ambiguity. *Behaviour Research and Therapy, 37*(5), 463-474.

Lecompte, D., Kaufman, L., Rousseeuw, P., & Tassin, A. (1983). Search for the relationship between academic performance and some psychosocial factors. The use of a structured interview. *Acta Psychiatrica Belgica, 83*(6), 598-608.

Lecrubier, Y., Sheehan, D., Weiller, E., Amorim, P., Bonora, I., Harnett Sheehan, K., . . . Dunbar, G. (1997). The Mini International Neuropsychiatric Interview (MINI). A short diagnostic structured interview: Reliability and validity according to the CIDI. *European Psychiatry, 12*(5), 224-231.

Lee, J., & Park, S. (2005). Working memory impairments in schizophrenia: A meta-analysis. *Journal of Abnormal Psychology, 114*(4), 599.

Lee, K. H., Choi, Y. Y., Gray, J. R., Cho, S. H., Chae, J., Lee, S., & Kim, K. (2006). Neural correlates of superior intelligence: Stronger recruitment of posterior parietal cortex. *Neuroimage, 29*(2), 578-586.

Lemelin, S., Baruch, P., Vincent, A., Laplante, L., Everett, J., & Vincent, P. (1996). Attention disturbance in clinical depression deficient distractor inhibition or processing resource deficit? *The Journal of Nervous and Mental Disease, 184*(2), 114-121.

Lens, W., & Decruyenaere, M. (1991). Motivation and de-motivation in secondary education: Student characteristics. *Learning and Instruction, 1*(2), 145-159.

Levens, S. M., & Gotlib, I. H. (2010). Updating positive and negative stimuli in working memory in depression. *Journal of Experimental Psychology: General, 139*(4), 654.

Levenstein, S., Prantera, C., Varvo, V., Scribano, M. L., Berto, E., Luzi, C., & Andreoli, A. (1993). Development of the Perceived Stress Questionnaire: A new tool for psychosomatic research. *Journal of Psychosomatic Research, 37*(1), 19-32.

Li, S., Schmiedek, F., Huxhold, O., Röcke, C., Smith, J., & Lindenberger, U. (2008). Working memory plasticity in old age: Practice gain, transfer, and maintenance. *Psychology and Aging, 23*(4), 731.

Linden, D. E. (2007). The working memory networks of the human brain. *The Neuroscientist: A Review Journal Bringing Neurobiology, Neurology and Psychiatry, 13*(3), 257-267. doi:10.1177/1073858406298480

Linville, P. (1996). Attention inhibition: Does it underlie ruminative thought. *Advances in Social Cognition, 9*, 121-133.

Locke, E. A. (1968). Toward a theory of task motivation and incentives. *Organizational Behavior and Human Performance, 3*(2), 157-189.

Lockwood, K. A., Alexopoulos, G. S., & van Gorp, W. G. (2002). Executive dysfunction in geriatric depression. *American Journal of Psychiatry, 159*(7), 1119-1126.

Loosli, S. V., Buschkuehl, M., Perrig, W. J., & Jaeggi, S. M. (2012). Working memory training improves reading processes in typically developing children. *Child Neuropsychology, 18*(1), 62-78.

Love, A., James, D., & Willner, P. (1998). A comparison of two alcohol craving questionnaires. *Addiction, 93*(7), 1091-1102.

Lubin, B. (1965). Adjective checklists for measurement of depression. *Archives of General Psychiatry, 12*(1), 57-62.

Luciana, M., Depue, R. A., Arbisi, P., & Leon, A. (1992). Facilitation of working memory in humans by a D2 dopamine receptor agonist. *Journal of Cognitive Neuroscience, 4*(1), 58-68.

Lumley, F., & Calhoun, S. (1934). Memory span for words presented auditorially. *Journal of Applied Psychology, 18*(6), 773.

Lundqvist, T. (2005). Cognitive consequences of cannabis use: Comparison with abuse of stimulants and heroin with regard to attention, memory and executive functions. *Pharmacology Biochemistry and Behavior, 81*(2), 319-330.

Lyubomirsky, S., Kasri, F., & Zehm, K. (2003). Dysphoric rumination impairs concentration on academic tasks. *Cognitive Therapy and Research, 27*(3), 309-330.

Lyubomirsky, S., & Nolen-Hoeksema, S. (1995). Effects of self-focused rumination on negative thinking and interpersonal problem solving. *Journal of Personality and Social Psychology, 69*(1), 176.

MacLeod, C., & Donnellan, A. M. (1993). Individual differences in anxiety and the restriction of working memory capacity. *Personality and Individual Differences, 15*(2), 163-173.

MacLeod, C., & Mathews, A. (1988). Anxiety and the allocation of attention to threat. *The Quarterly Journal of Experimental Psychology, 40*(4), 653-670.

MacQueen, G. M., Tipper, S., Young, L., Joffe, R., & Levitt, A. (2000). Impaired distractor inhibition on a selective attention task in unmedicated, depressed subjects. *Psychological Medicine, 30*(03), 557-564.

Magill, M., & Ray, L. A. (2009). Cognitive-behavioral treatment with adult alcohol and illicit drug users: A meta-analysis of randomized controlled trials. *Journal of Studies on Alcohol and Drugs, 70*(4), 516-527.

Mathews, A., & MacLeod, C. (1985). Selective processing of threat cues in anxiety states. *Behaviour Research and Therapy, 23*(5), 563-569.

Mathews, A., & MacLeod, C. (1994). Cognitive approaches to emotion and emotional disorders. *Annual Review of Psychology, 45*(1), 25-50.

Mathews, A., & Mackintosh, B. (1998). A cognitive model of selective processing in anxiety. *Cognitive Therapy and Research, 22*(6), 539-560.

McCarthy, G., Puce, A., Constable, R. T., Krystal, J. H., Gore, J. C., & Goldman-Rakic, P. (1996). Activation of human prefrontal cortex during spatial and nonspatial working memory tasks measured by functional MRI. *Cerebral Cortex, 6*(4), 600-611.

McCrady, B. S., & Smith, D. E. (1986). Implications of cognitive impairment for the treatment of alcoholism. *Alcoholism: Clinical and Experimental Research, 10*(2), 145-149.

McCrone, P., Knapp, M., Proudfoot, J., Ryden, C., Cavanagh, K., Shapiro, D. A., . . . Tylee, A. (2004). Cost-effectiveness of computerised cognitive-behavioural therapy for anxiety and depression in primary care: Randomised controlled trial. *The British Journal of Psychiatry, 185*, 55-62.

McLellan, A. T., Luborsky, L., Woody, G. E., & O'Brien, C. P. (1980). An improved diagnostic evaluation instrument for substance abuse patients: The Addiction Severity Index. *The Journal of Nervous and Mental Disease, 168*(1), 26-33.

McNab, F., & Klingberg, T. (2008). Prefrontal cortex and basal ganglia control access to working memory. *Nature Neuroscience, 11*(1), 103-107.

McNab, F., Varrone, A., Farde, L., Jucaite, A., Bystritsky, P., Forssberg, H., & Klingberg, T. (2009). Changes in cortical dopamine D1 receptor binding associated with cognitive training. *Science, 323*(5915), 800-802. doi:10.1126/science.1166102; 10.1126/science.1166102

McNally, R. J., Lasko, N. B., Macklin, M. L., & Pitman, R. K. (1995). Autobiographical memory disturbance in combat-related posttraumatic stress disorder. *Behaviour Research and Therapy, 33*(6), 619-630.

Melby-Lervåg, M., & Hulme, C. (2013). Is working memory training effective? A meta-analytic review. *Developmental Psychology, 49*(2), 270.

Mesulam, M. M. (1998). From sensation to cognition. *Brain, 121*, 1013-1052.

Michalak, J., Hölz, A., & Teismann, T. (2011). Rumination as a predictor of relapse in mindfulness-based cognitive therapy for depression. *Psychology and Psychotherapy: Theory, Research and Practice, 84*(2), 230-236. doi:10.1348/147608310X520166

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*(1), 167-202.

Millisecond Software. (2003). Inquisit (3). Seattle, WA: Millisecond Software.

Mitte, K. (2005). Meta-analysis of cognitive-behavioral treatments for generalized anxiety disorder: A comparison with pharmacotherapy. *Psychological Bulletin, 131*(5), 785.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology, 41*(1), 49-100.

Miyake, A., & Shah, P. (1999). *Models of working memory: Mechanisms of active maintenance and executive control*. New York, NY: Cambridge University Press.

Moeller, F. G., Barratt, E. S., Dougherty, D. M., Schmitz, J. M., & Swann, A. C. (2001). Psychiatric aspects of impulsivity. *American Journal of Psychiatry, 158*(11), 1783-1793.

Monsell, S. (1996). Control of mental processes. In V. Bruce (Ed.), *Unsolved mysteries of the mind: Tutorial essays in cognition* (pp. 93-148). Oxford: Erlbaum Taylor & Francis.

Moore, M. E., & Ross, B. M. (1963). Context effects in running memory. *Psychological Reports, 12*(2), 451-465.

Mor, N., & Winquist, J. (2002). Self-focused attention and negative affect: A meta-analysis. *Psychological Bulletin, 128*(4), 638.

Moritz, S., Birkner, C., Kloss, M., Jacobsen, D., Fricke, S., Böthern, A., & Hand, I. (2001). Impact of comorbid depressive symptoms on neuropsychological performance in obsessive-compulsive disorder. *Journal of Abnormal Psychology, 110*(4), 653.

Morris, N., & Jones, D. M. (1990). Memory updating in working memory: The role of the central executive. *British Journal of Psychology, 81*(2), 111-121.

Morrison, A. B., & Chein, J. M. (2011). Does working memory training work? The promise and challenges of enhancing cognition by training working memory. *Psychonomic Bulletin & Review, 18*(1), 46-60.

Muller, U., von Cramon, D. Y., & Pollmann, S. (1998). D1- versus D2-receptor modulation of visuospatial working memory in humans. *The Journal of Neuroscience, 18*(7), 2720-2728.

Murphy, F., Sahakian, B., Rubinsztein, J., Michael, A., Rogers, R., Robbins, T., & Paykel, E. (1999). Emotional bias and inhibitory control processes in mania and depression. *Psychological Medicine, 29*(6), 1307-1321.

Murphy, F. C., Rubinsztein, J. S., Michael, A., Rogers, R. D., Robbins, T. W., Paykel, E. S., & Sahakian, B. J. (2001). Decision-making cognition in mania and depression. *Psychological Medicine, 31*(4), 679-693.

Murray, C. J., & Lopez, A. D. (1997). Alternative projections of mortality and disability by cause 1990–2020: Global burden of disease study. *The Lancet, 349*(9064), 1498-1504.

Nationaal Kompas Volksgezondheid. (2013). Hoe vaak komen stemmingsstoornissen voor en hoeveel mensen sterven er aan? Retrieved 2014, retrieved from http://www.nationaalkompas.nl/gezondheid-en-ziekte/ziekten-en-aandoeningen/psychische-stoornissen/depressie/omvang/

Nee, D. E., & Jonides, J. (2008). Dissociable interference-control processes in perception and memory. *Psychological Science, 19*(5), 490-500. doi:10.1111/j.1467-9280.2008.02114.x; 10.1111/j.1467-9280.2008.02114.x

Neubauer, A. C., Bergner, S., & Schatz, M. (2010). Two- vs. three-dimensional presentation of mental rotation tasks: Sex differences and effects of training on performance and brain activation. *Intelligence, 38*(5), 529-539.

Neubauer, A. C., & Fink, A. (2009). Intelligence and neural efficiency. *Neuroscience & Biobehavioral Reviews, 33*(7), 1004-1023.

Nigg, J. T., Wong, M. M., Martel, M. M., Jester, J. M., Puttler, L. I., Glass, J. M., . . . Zucker, R. A. (2006). Poor response inhibition as a predictor of problem drinking and illicit drug use in adolescents at risk for alcoholism and other substance use disorders. *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(4), 468-475.

Noël, X., Bechara, A., Dan, B., Hanak, C., & Verbanck, P. (2007). Response inhibition deficit is involved in poor decision making under risk in nonamnesic individuals with alcoholism. *Neuropsychology, 21*(6), 778.

Nolen-Hoeksema, S. (2000). The role of rumination in depressive disorders and mixed anxiety/depressive symptoms. *Journal of Abnormal Psychology, 109*(3), 504.

Nolen-Hoeksema, S., & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster: The 1989 Loma Prieta earthquake. *Journal of Personality and Social Psychology, 61*(1), 115.

Norman, D. A., & Shallice, T. (1986). *Attention to action* Springer.

O'Brien, C. P. (2006). Drug addiction and rug abuse. In L. Brunton, J. Lazo & K. Parker (Eds.), *Goodman & Gillman's the pharmacological basis of therapeutics* (11th ed., pp. 607-627). New York, NY: McGraw-Hill.

Okada, G., Okamoto, Y., Morinobu, S., Yamawaki, S., & Yokota, N. (2003). Attenuated left prefrontal activation during a verbal fluency task in patients with depression. *Neuropsychobiology, 47*(1), 21-26. doi:68871

Olesen, P. J., Westerberg, H., & Klingberg, T. (2004). Increased prefrontal and parietal activity after training of working memory. *Nature Neuroscience, 7*(1), 75-79.

Olesen, P. J., Macoveanu, J., Tegner, J., & Klingberg, T. (2007). Brain activity related to working memory and distraction in children and adults. *Cerebral Cortex, 17*(5), 1047-1054. doi:10.1093/cercor/bhl014

Olesen, P. J., Nagy, Z., Westerberg, H., & Klingberg, T. (2003). Combined analysis of DTI and fMRI data reveals a joint maturation of white and grey matter in a fronto-parietal network. *Cognitive Brain Research, 18*(1), 48-57.

Onraedt, T., & Koster, E. H. (2014). Training working memory to reduce rumination. *PloS One, 9*(3), e90632.

Onraedt, T., Koster, E., Geraerts, E., De Lissnyder, E., & De Raedt, R. (2011). Werkgeheugen en depressie: Van het lab naar het spreekuur. *De Psycholoog, 46*(11), 14-23.

Orne, M. T., & Scheibe, K. E. (1964). The contribution of nondeprivation factors in the production of sensory deprivation effects: The psychology of the "panic button". *The Journal of Abnormal and Social Psychology, 68*(1), 3.

Ouimet, A. J., Gawronski, B., & Dozois, D. J. (2009). Cognitive vulnerability to anxiety: A review and an integrative model. *Clinical Psychology Review, 29*(6), 459-470.

Owens, M., & Derakshan, N. (2013). The effects of dysphoria and rumination on cognitive flexibility and task selection. *Acta Psychologica, 142*(3), 323-331.

Owens, M., Koster, E. H., & Derakshan, N. (2013). Improving attention control in dysphoria through cognitive training: Transfer effects on working memory capacity and filtering efficiency. *Psychophysiology, 50*(3), 297-307.

Padula, C. B., Schweinsburg, A. D., & Tapert, S. F. (2007). Spatial working memory performance and fMRI activation interaction in abstinent adolescent marijuana users. *Psychology of Addictive Behaviors, 21*(4), 478.

Paelecke-Habermann, Y., Pohl, J., & Leplow, B. (2005). Attention and executive functions in remitted major depression patients. *Journal of Affective Disorders, 89*(1), 125-135.

Palmer, B. W., Boone, K. B., Lesser, I. M., Wohl, M. A., Berman, N., & Miller, B. L. (1996). Neuropsychological deficits among older depressed patients with predominantly psychological or vegetative symptoms. *Journal of Affective Disorders, 41*(1), 17-24.

Pascual-Leone, A., Rubio, B., Pallardó, F., & Catalá, M. D. (1996). Rapid-rate transcranial magnetic stimulation of left dorsolateral prefrontal cortex in drug-resistant depression. *The Lancet, 348*(9022), 233-237.

Patton, J. H., & Stanford, M. S. (1995). Factor structure of the Barratt Impulsiveness Scale. *Journal of Clinical Psychology, 51*(6), 768-774.

Penninx, B. W., Nolen, W. A., Lamers, F., Zitman, F. G., Smit, J. H., Spinhoven, P., . . . van der Meer, K. (2011). Two-year course of depressive and anxiety disorders: Results from the Netherlands Study of Depression and Anxiety (NESDA). *Journal of Affective Disorders, 133*(1), 76-85.

Perrig, W. J., Hollenstein, M., & Oelhafen, S. (2009). Can we improve fluid intelligence with training on working memory in persons with intellectual disabilities? *Journal of Cognitive Education and Psychology, 8*(2), 148-164.

Perry, J. L., & Carroll, M. E. (2008). The role of impulsive behavior in drug abuse. *Psychopharmacology, 200*(1), 1-26.

Peyrot, W. J., Middeldorp, C. M., Jansen, R., Smit, J. H., de Geus, E. J., Hottenga, J., . . . Barragan, I. (2013). Strong effects of environmental factors on prevalence and course of major depressive disorder are not moderated by 5-HTTLPR polymorphisms in a large Dutch sample. *Journal of Affective Disorders, 146*(1), 91-99.

Philippot, P., & Brutoux, F. (2008). Induced rumination dampens executive processes in dysphoric young adults. *Journal of Behavior Therapy and Experimental Psychiatry, 39*(3), 219-227.

Polivy, J., & Doyle, C. (1980). Laboratory induction of mood states through the reading of self-referent mood statements: Affective changes or demand characteristics? *Journal of Abnormal Psychology, 89*(2), 286.

Pollack, I., Johnson, L. B., & Knaff, P. R. (1959). Running memory span. *Journal of Experimental Psychology, 57*(3), 137.

Pollock, L. R., & Williams, J. M. G. (2001). Effective problem solving in suicide attempters depends on specific autobiographical recall. *Suicide and Life-Threatening Behavior, 31*(4), 386-396.

Pope, H. G., Gruber, A. J., Hudson, J. I., Huestis, M. A., & Yurgelun-Todd, D. (2001). Neuropsychological performance in long-term cannabis users. *Archives of General Psychiatry, 58*(10), 909-915.

Porter, R. J., Gallagher, P., Thompson, J. M., & Young, A. H. (2003). Neurocognitive impairment in drug-free patients with major depressive disorder. *The British Journal of Psychiatry, 182*, 214-220.

Prins, P. J., Dovis, S., Ponsioen, A., Ten Brink, E., & van der Oord, S. (2011). Does computerized working memory training with game elements enhance motivation and

training efficacy in children with ADHD? *Cyberpsychology, Behavior, and Social Networking, 14*(3), 115-122.

Proudfoot, J. G. (2004). Computer-based treatment for anxiety and depression: Is it feasible? Is it effective? *Neuroscience & Biobehavioral Reviews, 28*(3), 353-363.

Raes, F., Hermans, D., & Eelen, P. (2003). Kort instrumenteel de Nederlandstalige versie van de Ruminative Response Scale (RRS-NL) en de Rumination on Sadness Scale (RSS-NL). *Gedragstherapie, 36*(2), 97-104.

Raes, F., Hermans, D., Williams, J. M. G., & Eelen, P. (2007). A sentence completion procedure as an alternative to the autobiographical memory test for assessing overgeneral memory in non-clinical populations. *Memory, 15*(5), 495-507.

Raes, F., Schoofs, H., Hoes, D., Hermans, D., Van Den Eede, F., & Franck, E. (2009). 'Reflection' en 'brooding' als subtypes van rumineren: Een herziening van de Ruminative Response Scale. *Gedragstherapie, 42*(3/4), 205-214.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences of the United States of America, 98*(2), 676-682. doi:10.1073/pnas.98.2.676

Ramsawh, H., Raffa, S., Edelen, M. O., Rende, R., & Keller, M. (2009). Anxiety in middle adulthood: Effects of age and time on the 14-year course of panic disorder, social phobia and generalized anxiety disorder. *Psychological Medicine, 39*(4), 615.

Rapee, R. M. (1993). The utilisation of working memory by worry. *Behaviour Research and Therapy, 31*(6), 617-620.

Ratti, M., Bo, P., Giardini, A., & Soragna, D. (2002). Chronic alcoholism and the frontal lobe: Which executive functions are impaired? *Acta Neurologica Scandinavica, 105*(4), 276-281.

Ravnkilde, B., Videbech, P., Clemmensen, K., Egander, A., Rasmussen, N. A., & Rosenberg, R. (2002). Cognitive deficits in major depression. *Scandinavian Journal of Psychology, 43*(3), 239-251.

Redick, T. S., Shipstead, Z., Harrison, T. L., Hicks, K. L., Fried, D. E., Hambrick, D. Z., . . . Engle, R. W. (2013). No evidence of intelligence improvement after working memory training: A randomized, placebo-controlled study. *Journal of Experimental Psychology: General, 142*(2), 359.

Repovš, G., & Baddeley, A. (2006). The multi-component model of working memory: Explorations in experimental cognitive psychology. *Neuroscience, 139*(1), 5-21.

Reynolds, M., & Brewin, C. R. (1999). Intrusive memories in depression and posttraumatic stress disorder. *Behaviour Research and Therapy, 37*(3), 201-215.

Richell, R. A., & Anderson, M. (2004). Reproducibility of negative mood induction: A self-referent plus musical mood induction procedure and a controllable/uncontrollable stress paradigm. *Journal of Psychopharmacology, 18*(1), 94-101. doi:10.1177/0269881104040246

Richmond, R. (1992). Discriminating variables among psychotherapy dropouts from a psychological training clinic. *Professional Psychology: Research and Practice, 23*(2), 123.

Ridder, D., de, & Schreurs, K. (2001). Developing interventions for chronically ill patients: Is coping a helpful concept? *Clinical Psychology Review, 21*(2), 205-240.

Robbins, T., Roberts, A., Owen, A., Sahakian, B., Everitt, B., Wilkinson, L., . . . Tovee, M. (1994). Monoaminergic-dependent cognitive functions of the prefrontal cortex in monkey and man. In A. M. Thierry (Ed.), *Motor and cognitive functions of the prefrontal cortex* (pp. 93-111). Berlin: Springer.

Roberts, J. E., Gilboa, E., & Gotlib, I. H. (1998). Ruminative response style and vulnerability to episodes of dysphoria: Gender, neuroticism, and episode duration. *Cognitive Therapy and Research, 22*(4), 401-423.

Robertson, L., Smith, M., Castle, D., & Tannenbaum, D. (2006). Using the internet to enhance the treatment of depression. *Australasian Psychiatry, 14*(4), 413-417.

Rogers, M. A., Kasai, K., Koji, M., Fukuda, R., Iwanami, A., Nakagome, K., . . . Kato, N. (2004). Executive and prefrontal dysfunction in unipolar depression: A review of neuropsychological and imaging evidence. *Neuroscience Research, 50*(1), 1-11.

Rogers, R. D., & Monsell, S. (1995). Costs of a predictible switch between simple cognitive tasks. *Journal of Experimental Psychology: General, 124*(2), 207.

Roozen, H. G., Boulogne, J. J., van Tulder, M. W., van den Brink, W., de Jong, C. A., & Kerkhof, A. J. (2004). A systematic review of the effectiveness of the community reinforcement approach in alcohol, cocaine and opioid addiction. *Drug and Alcohol Dependence, 74*(1), 1-13.

Rosen, V. M., & Engle, R. W. (1998). Working memory capacity and suppression. *Journal of Memory and Language, 39*(3), 418-436.

Rusting, C. L. (1998). Personality, mood, and cognitive processing of emotional information: Three conceptual frameworks. *Psychological Bulletin, 124*(2), 165.

Sanderman, R., & Ormel, J. (1992). De Utrechtse Coping Lijst (UCL): Validiteit en betrouwbaarheid. *Gedrag En Gezondheid, 20*(32), 7.

Saunders, J. B., Aasland, O. G., Babor, T. F., de la Fuente, Juan R, & Grant, M. (1993). Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. *Addiction, 88*(6), 791-804.

Schacter, D. L., Wig, G. S., & Stevens, W. D. (2007). Reductions in cortical activity during priming. *Current Opinion in Neurobiology, 17*(2), 171-176.

Scherer, R. W., Langenberg, P., & Von Elm, E. (2007). Full publication of results initially presented in abstracts. *Cochrane Database of Systematic Reviews, 2*(2)

Scherf, K. S., Sweeney, J. A., & Luna, B. (2006). Brain basis of developmental change in visuospatial working memory. *Journal of Cognitive Neuroscience, 18*(7), 1045-1058.

Schippers, G., de Jong, C., Lehert, P., Potgieter, A., Deckers, F., Casselman, J., & Geerlings, P. (1997). The Obsessive Compulsive Drinking Scale: Translation into Dutch and possible modifications. *European Addiction Research, 3*(3), 116-122.

Schmand, B., Kuipers, T., van der Gaag, M., Bosveld, J., Bulthuis, F., & Jellema, M. (1994). Cognitive disorders and negative symptoms as correlates of motivational deficits in psychotic patients. *Psychological Medicine, 24*(4), 869-884.

Schmeichel, B. J., Volokhov, R. N., & Demaree, H. A. (2008). Working memory capacity and the self-regulation of emotional expression and experience. *Journal of Personality and Social Psychology, 95*(6), 1526.

Schmiedek, F., Lovden, M., & Lindenberger, U. (2010). Hundred days of cognitive training enhance broad cognitive abilities in adulthood: Findings from the COGITO study. *Frontiers in Aging Neuroscience, 2* doi:10.3389/fnagi.2010.00027; 10.3389/fnagi.2010.00027

Schotte, C., Maes, M., Cluydts, R., De Doncker, D., & Cosyns, P. (1997). Construct validity of the Beck Depression Inventory in a depressive population. *Journal of Affective Disorders, 46*(2), 115-125.

Schreurs, P. J. G., van de Willige, G., Brosschot, J. F., Tellegen, B., & Graus, G. M. H. (1993). *De Utrechtse Coping Lijst: UCL. Omgaan met problemen en gebeurtenissen, herziene handleiding. [the Utrecht's Coping List: UCL. Managing problems and events, revised manual]*. Lisse: Swets Test Publishers.

Schuckit, M. A. (2006). Comorbidity between substance use disorders and psychiatric conditions. *Addiction, 101*, 76-88.

Schweinsburg, A. D., Nagel, B. J., Schweinsburg, B. C., Park, A., Theilmann, R. J., & Tapert, S. F. (2008). Abstinent adolescent marijuana users show altered fMRI response during spatial working memory. *Psychiatry Research, 163*(1), 40-51.

Schweizer, S., Grahn, J., Hampshire, A., Mobbs, D., & Dalgleish, T. (2013). Training the emotional brain: Improving affective control through emotional working memory training. *The Journal of Neurosciene, 33*(12), 5301-5311.

Segerstrom, S. C., Tsao, J. C., Alden, L. E., & Craske, M. G. (2000). Worry and rumination: Repetitive thought as a concomitant and predictor of negative mood. *Cognitive Therapy and Research, 24*(6), 671-688.

Seibert, P. S., & Ellis, H. C. (1991). A convenient self-referencing mood induction procedure. *Bulletin of the Psychonomic Society, 29*(2), 121-124.

Shadish, W. R., Cook, T. D., & Campbell, D. T. (2002). *Experimental and quasi-experimental designs for generalized causal inference*. Boston, MA: Houghton Mifflin.

Shamosh, N. A., Deyoung, C. G., Green, A. E., Reis, D. L., Johnson, M. R., Conway, A. R., . . . Gray, J. R. (2008). Individual differences in delay discounting: Relation to intelligence, working memory, and anterior prefrontal cortex. *Psychological Science, 19*(9), 904-911. doi:10.1111/j.1467-9280.2008.02175.x; 10.1111/j.1467-9280.2008.02175.x

Sheehan, D., Janavs, J., Baker, R., Harnett-Sheehan, K., Knapp, E., Sheehan, M., . . . Amorim, P. (1998). MINI - Mini International Neuropsychiatric Interview - English version 5.0.0-DSM-IV. *Journal of Clinical Psychiatry, 59*, 34-57.

Sheline, Y. I., Barch, D. M., Price, J. L., Rundle, M. M., Vaishnavi, S. N., Snyder, A. Z., . . . Raichle, M. E. (2009). The default mode network and self-referential processes in

depression. *Proceedings of the National Academy of Sciences of the United States of America, 106*(6), 1942-1947. doi:10.1073/pnas.0812686106; 10.1073/pnas.0812686106

Shipstead, Z., Redick, T. S., & Engle, R. W. (2010). Does working memory training generalize? *Psychologica Belgica, 50*(3-4), 3-4.

Shipstead, Z., Redick, T. S., & Engle, R. W. (2012). Is working memory training effective? *Psychological Bulletin, 138*(4), 628.

Siegle, G. J., Ghinassi, F., & Thase, M. E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research, 31*(2), 235-262.

Siemer, M. (2005). Mood-congruent cognitions constitute mood experience. *Emotion, 5*(3), 296.

Silverman, K., DeFulio, A., & Sigurdsson, S. O. (2012). Maintenance of reinforcement to address the chronic nature of drug addiction. *Preventive Medicine, 55*, S46-S53.

Smith, A. M., Longo, C. A., Fried, P. A., Hogan, M. J., & Cameron, I. (2010). Effects of marijuana on visuospatial working memory: An fMRI study in young adults. *Psychopharmacology, 210*(3), 429-438.

Smith, E. E., & Jonides, J. (1997). Working memory: A view from neuroimaging. *Cognitive Psychology, 33*(1), 5-42.

Soares, J. C., & Mann, J. J. (1997). The anatomy of mood disorders - review of structural neuroimaging studies. *Biological Psychiatry, 41*(1), 86-106.

Sobin, C., & Sackeim, H. A. (1997). Psychomotor symptoms of depression. *The American Journal of Psychiatry, 154*(1), 4-17.

Solowij, N., Stephens, R. S., Roffman, R. A., Babor, T., Kadden, R., Miller, M., . . . Vendetti, J. (2002). Cognitive functioning of long-term heavy cannabis users seeking treatment. *Journal of the American Medical Association, 287*(9), 1123-1131.

Sonawalla, S. B., Farabaugh, A. H., Leslie, V. M., Pava, J. A., Matthews, J. D., & Fava, M. (2002). Early drop-outs, late drop-outs and completers: Differences in the continuation phase of a clinical trial. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 26*(3), 415-419.

Sorg, B. A., & Whitney, P. (1992). The effect of trait anxiety and situational stress on working memory capacity. *Journal of Research in Personality, 26*(3), 235-241.

Spielberger, C. D., Gorsuch, R. L., Lushene, R. E., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the State-Trait Anxiety Inventory.* Palo Alto, CA: Consulting psychologists press.

Spijker, J., de Graaf, R., Bijl, R. V., Beekman, A. T., Ormel, J., & Nolen, W. A. (2002). Duration of major depressive episodes in the general population: Results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *The British Journal of Psychiatry, 181*, 208-213.

Strauss, G. P., Allen, D. N., Jorgensen, M. L., & Cramer, S. L. (2005). Test-retest reliability of standard and emotional stroop tasks: An investigation of color-word and picture-word versions. *Assessment, 12*(3), 330-337. doi:10.1177/1073191105276375

Stroemer, R. P., Kent, T. A., & Hulsebosch, C. E. (1998). Enhanced neocortical neural sprouting, synaptogenesis, and behavioral recovery with D-amphetamine therapy after neocortical infarction in rats. *Stroke, 29*(11), 2381-2395.

Subramaniam, K., Luks, T. L., Fisher, M., Simpson, G. V., Nagarajan, S., & Vinogradov, S. (2012). Computerized cognitive training restores neural activity within the reality monitoring network in schizophrenia. *Neuron, 73*(4), 842-853.

Svanborg, P., & Åsberg, M. (2001). A comparison between the Beck Depression Inventory (BDI) and the self-rating version of the Montgomery Åsberg Depression Rating Scale (MADRS). *Journal of Affective Disorders, 64*(2), 203-216.

Sweeney, J. A., Kmiec, J. A., & Kupfer, D. J. (2000). Neuropsychologic impairments in bipolar and unipolar mood disorders on the CANTAB neurocognitive battery. *Biological Psychiatry, 48*(7), 674-684.

Szulecka, T. K., Springett, N. R., & de Pauw, K. W. (1987). General health, psychiatric vulnerability and withdrawal from university in first-year undergraduates. *British Journal of Guidance and Counselling, 15*(1), 82-91.

Takeuchi, H., Taki, Y., & Kawashima, R. (2010). Effects of working memory training on cognitive functions and neural systems. *Reviews in the Neurosciences, 21*(6), 427-450.

Tangney, J. P., Baumeister, R. F., & Boone, A. L. (2004). High self-control predicts good adjustment, less pathology, better grades, and interpersonal success. *Journal of Personality, 72*(2), 271-324.

Tavares, J. T., Drevets, W., & Sahakian, B. (2003). Cognition in mania and depression. *Psychological Medicine, 33*(06), 959-967.

Taylor, D. R., Poulton, R., Moffitt, T. E., Ramankutty, P., & Sears, M. R. (2000). The respiratory effects of cannabis dependence in young adults. *Addiction, 95*(11), 1669-1677.

Taylor, J. A. (1953). A personality scale of manifest anxiety. *The Journal of Abnormal and Social Psychology, 48*(2), 285.

Thorell, L. B., Lindqvist, S., Nutley, S. B., Bohlin, G., & Klingberg, T. (2009). Training and transfer effects of executive functions in preschool children. *Developmental Science, 12*(1), 106-113.

Thormählen, B., Weinryb, R. M., Norén, K., Vinnars, B., Bagedahl-Strindlund, M., & Barber, J. P. (2003). Patient factors predicting dropout from supportive-expressive psychotherapy for patients with personality disorders. *Psychotherapy Research, 13*(4), 493-509.

Todd, J. J., & Marois, R. (2004). Capacity limit of visual short-term memory in human posterior parietal cortex. *Nature, 428*(6984), 751-754.

Treynor, W., Gonzalez, R., & Nolen-Hoeksema, S. (2003). Rumination reconsidered: A psychometric analysis. *Cognitive Therapy and Research*, *27*(3), 247-259.

Trichard, C., Martinot, J., Alagille, M., Masure, M., Hardy, P., Ginestet, D., & Feline, A. (1995). Time course of prefrontal lobe dysfunction in severely depressed in-patients: A longitudinal neuropsychological study. *Psychological Medicine, 25*(1), 79-86.

Unsworth, N., & Engle, R. W. (2006). Simple and complex memory spans and their relation to fluid abilities: Evidence from list-length effects. *Journal of Memory and Language, 54*(1), 68-80.

Unsworth, N., & Engle, R. W. (2007). The nature of individual differences in working memory capacity: Active maintenance in primary memory and controlled search from secondary memory. *Psychological Review, 114*(1), 104.

Unsworth, N., Heitz, R. P., Schrock, J. C., & Engle, R. W. (2005). An automated version of the operation span task. *Behavior Research Methods, 37*(3), 498-505.

Unsworth, N., Redick, T. S., Heitz, R. P., Broadway, J. M., & Engle, R. W. (2009). Complex working memory span tasks and higher-order cognition: A latent-variable analysis of the relationship between processing and storage. *Memory, 17*(6), 635-654.

Unsworth, N., & Spillers, G. J. (2010). Working memory capacity: Attention control, secondary memory, or both? A direct test of the dual-component model. *Journal of Memory and Language, 62*(4), 392-406.

Ursin, H. (2005). Press stop to start: The role of inhibition for choice and health. *Psychoneuroendocrinology, 30*(10), 1059-1065.

Van den Brink, W. (2009). Geschiedenis en classificatie. In I. Franken, & W. Van Den Brink (Eds.), *Handboek verslaving* (1st ed.,). Utrecht: De Tijdstroom.

Van der Does, A. J. W. (2002). *BDI-II-NL: Handleiding Beck Depression Inventory-II, Nederlandse vertaling en bewerking [BDI-II-NL: Manual Beck Depression Inventory-II, Dutch translation and adaptation]*. Lisse: Swets Test Publisher.

Van der Molen, M., van Luit, J., van der Molen, M., Klugkist, I., & Jongmans, M. (2010). Effectiveness of a computerised working memory training in adolescents with mild to borderline intellectual disabilities. *Journal of Intellectual Disability Research, 54*(5), 433-447.

Van der Ploeg, E., Mooren, T., Kleber, R., J., van der Velden, P. G., & Brom, D. (2004). Construct validation of the Dutch version of the Impact of Event Scale. *Psychological Assessment, 16*(1), 16.

Van der Ploeg, H., Defares, P., & Spielberger, C. (Eds.). (1979). *Handleiding bij de Zelf-Beoordelings Vragenlijst (ZBV): Een Nederlandse bewerking van de State-Trait Anxiety Inventory [manual of the Dutch State-Trait Anxiety Inventory]*. Lisse: Swets en Zeitlinger.

Van Gageldonk, A., Rigter, H., Ketelaars, T., & van Laar, M. (2005). Kansvolle psychosociale behandelingen voor problemen met illegale drugs. *Verslaving, 1*(2), 62-69.

Van Kerkhof, M. (2006). Van craving en ADHD tot opvoedingsondersteuning: De stand van zaken in de wetenschap over verslaving. *Verslaving, 2*(3), 122-126.

Van Laar, M. (2009). Epidemiologie. In I. H. A. Franken, & W. Van den Brink (Eds.), *Handboek verslaving* (pp. 27-49). Utrecht: De Tijdstroom.

Van Rooij, A. J., Schoenmakers, T. M., Van de Mheen, D. (2011) Nationaal Prevalentie Onderzoek Middelengebruik 2009: De kerncijfers [National Prevalence Study on Substance Use 2009: Core Statistics]. Rotterdam, IVO.

Van 't Land, H., Schoemaker, C., & de Ruiter, C. (2008). *Trimbos zakboek psychische stoornissen.* (2nd and extended ed.). Utrecht: De Tijdstroom.

Van Vliet, I. M., Leroy, H., & van Megen, H. J. G. M. (2000). *Dutch version 5.0.0. of the MINI international neuropsychiatric interview*. Leiden: Leids Universitair Medisch Centrum.

Van Vreeswijk, M. F., & de Wilde, E. J. (2004). Autobiographical memory specificity, psychopathology, depressed mood and the use of the Autobiographical Memory Test: A meta-analysis. *Behaviour Research and Therapy, 42*(6), 731-743.

Van Wilgenburg, H. (2006). Farmacologie van cannabis. *Verslaving, 2*(4), 172-175.

Vanderhasselt, M., Brunoni, A. R., Loeys, T., Boggio, P. S., & De Raedt, R. (2013). Nosce te ipsum–Socrates revisited? Controlling momentary ruminative self-referent thoughts by neuromodulation of emotional working memory. *Neuropsychologia, 51*(13), 2581-2589.

Velten Jr, E. (1968). A laboratory task for induction of mood states. *Behaviour Research and Therapy, 6*(4), 473-482.

Verdejo-García, A., Lawrence, A. J., & Clark, L. (2008). Impulsivity as a vulnerability marker for substance-use disorders: Review of findings from high-risk research, problem gamblers and genetic association studies. *Neuroscience & Biobehavioral Reviews, 32*(4), 777-810.

Verwoerd, J., Wessel, I., & de Jong, P. J. (2009). Individual differences in experiencing intrusive memories: The role of the ability to resist proactive interference. *Journal of Behavior Therapy and Experimental Psychiatry, 40*(2), 189-201.

Videbech, P., Ravnkilde, B., Pedersen, T., Hartvig, H., Egander, A., Clemmensen, K., . . . Rosenberg, R. (2002). The Danish PET/depression project: Clinical symptoms and cerebral blood flow. A regions-of-interest analysis. *Acta Psychiatrica Scandinavica, 106*(1), 35-44.

Vijayraghavan, S., Wang, M., Birnbaum, S. G., Williams, G. V., & Arnsten, A. F. (2007). Inverted-U dopamine D1 receptor actions on prefrontal neurons engaged in working memory. *Nature Neuroscience, 10*(3), 376-384.

Vogel, E. K., & Machizawa, M. G. (2004). Neural activity predicts individual differences in visual working memory capacity. *Nature, 428*(6984), 748-751.

Vogt, A., Kappos, L., Calabrese, P., Stöcklin, M., Gschwind, L., Opwis, K., & Penner, I. (2009). Working memory training in patients with multiple sclerosis–comparison of two different training schedules. *Restorative Neurology and Neuroscience, 27*(3), 225-235.

Volkow, N. (2010). *Cocaine: Abuse and addiction.* US Department of Health and Human Services National Institutes of Health. National institute on drug abuse research report series.

Von Sydow, K., Lieb, R., Pfister, H., Höfler, M., & Wittchen, H. (2002). What predicts incident use of cannabis and progression to abuse and dependence?: A 4-year prospective examination of risk factors in a community sample of adolescents and young adults. *Drug and Alcohol Dependence, 68*(1), 49-64.

Wanmaker, S., Gerearts, E., & Franken, I. H. A. *A working memory training to decrease rumination in depressed and anxious individuals: A double-blind randomized controlled trial.* Manuscript submitted for publication.

Watkins, P. C., Mathews, A., Williamson, D. A., & Fuller, R. D. (1992). Mood-congruent memory in depression: Emotional priming or elaboration? *Journal of Abnormal Psychology, 101*(3), 581.

Watkins, E., & Brown, R. G. (2002). Rumination and executive function in depression: An experimental study. *Journal of Neurology, Neurosurgery, and Psychiatry, 72*(3), 400-402.

Watts, F. N., McKenna, F. P., Sharrock, R., & Trezise, L. (1986). Colour naming of phobia-related words. *British Journal of Psychology, 77*(1), 97-108.

Weingartner, H., Cohen, R. M., Murphy, D. L., Martello, J., & Gerdt, C. (1981). Cognitive processes in depression. *Archives of General Psychiatry, 38*(1), 42-47.

Weiss, D. S., & Marmar, C. R. (1997). The Impact Of Event Scale-revised. *Assessing Psychological Trauma and PTSD, 2*, 168-189.

Wenzlaff, R. M., & Bates, D. E. (1998). Unmasking a cognitive vulnerability to depression: How lapses in mental control reveal depressive thinking. *Journal of Personality and Social Psychology, 75*(6), 1559.

Wessel, I., Overwijk, S., Verwoerd, J., & de Vrieze, N. (2008). Pre-stressor cognitive control is related to intrusive cognition of a stressful film. *Behaviour Research and Therapy, 46*(4), 496-513.

Westerberg, H., Jacobaeus, H., Hirvikoski, T., Clevberger, P., Östensson, M., Bartfai, A., & Klingberg, T. (2007). Computerized working memory training after stroke - A pilot study. *Brain Injury, 21*(1), 21-29.

Westerberg, H., Hirvikoski, T., Forssberg, H., & Klingberg, T. (2004). Visuo-spatial working memory span: A sensitive measure of cognitive deficits in children with ADHD. *Child Neuropsychology, 10*(3), 155-161.

Westermann, R., Spies, K., Stahl, G., & Hesse, F. W. (1996). Relative effectiveness and validity of mood induction procedures: A meta-analysis. *European Journal of Social Psychology, 26*(4), 557-580.

Wexler, B. E., Anderson, M., Fulbright, R. K., & Gore, J. C. (2000). Preliminary evidence of improved verbal working memory performance and normalization of task-related frontal lobe activation in schizophrenia following cognitive exercises. *American Journal of Psychiatry, 157*(10), 1694-1697.

Whitmer, A. J., & Banich, M. T. (2007). Inhibition versus switching deficits in different forms of rumination. *Psychological Science, 18*(6), 546-553. doi:10.1111/j.1467-9280.2007.01936.x

Williams, G. V., & Goldman-Rakic, P. S. (1995). Modulation of memory fields by dopamine dl receptors in prefrontal cortex. *Nature,* (376), 572-575. doi:10.1038/376572a0

Williams, J. M. G., Barnhofer, T., Crane, C., Herman, D., Raes, F., Watkins, E., & Dalgleish, T. (2007). Autobiographical memory specificity and emotional disorder. *Psychological Bulletin, 133*(1), 122.

Williams, J. M., & Broadbent, K. (1986). Autobiographical memory in suicide attempters. *Journal of Abnormal Psychology, 95*(2), 144.

Williams, J. W., Mulrow, C. D., Chiquette, E., Noel, P. H., Aguilar, C., & Cornell, J. (2000). A systematic review of newer pharmacotherapies for depression in adults: Evidence report summary. *Annals of Internal Medicine, 132*(9), 743-756.

Wisselink, D. J., Kuijpers, W. G. T., & Mol, A. (2013). *Kerncijfers verslavingszorg 2012*. Houten: Stichting Informatievoorziening Zorg.

Woods, D. L., Kishiyama, M. M., Yund, E. W., Herron, T. J., Edwards, B., Poliva, O., . . . Reed, B. (2011). Improving digit span assessment of short-term verbal memory. *Journal of Clinical and Experimental Neuropsychology, 33*(1), 101-111.

World Health Organisation. (2008). The global burden of disease: 2004 update. Retrieved 2014, from http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf

Zakzanis, K., Leach, L., & Kaplan, E. (1998). On the nature and pattern of neurocognitive function in major depressive disorder. *Cognitive and Behavioral Neurology, 11*(3), 111-119.

Zetsche, U., & Joormann, J. (2011). Components of interference control predict depressive symptoms and rumination cross-sectionally and at six months follow-up. *Journal of Behavior Therapy and Experimental Psychiatry, 42*(1), 65-73.

Zhou, Y., Yu, C., Zheng, H., Liu, Y., Song, M., Qin, W., . . . Jiang, T. (2010). Increased neural resources recruitment in the intrinsic organization in major depression. *Journal of Affective Disorders, 121*(3), 220-230.

Nederlandse samenvatting

Summary in Dutch

In dit proefschrift onderzochten we of het vergroten van het werkgeheugen kan leiden tot een vermindering van psychopathologie en een verbetering van mentaal welzijn, academische prestatie en gerelateerde factoren. Eerst wordt de theoretische achtergrond kort uiteengezet, wat leidt tot de onderzoeksvragen van de verschillende studies. Hierna worden de bevindingen besproken, en tenslotte wordt een conclusie getrokken.

Achtergrond

De studies beschreven in **hoofdstuk 3 tot en met 5 en 7** richten zich op depressie, angststoornissen en alcohol-, cannabis- en cocaïneverslaving. Deze psychopathologie komt het meest voor in Nederland en treft respectievelijk 18,7%, 19,6% en 19,1% van de Nederlanders ooit tijdens het leven (De Graaf, ten Have, Van Gool, & Van Dorsselaer, 2012). Ondanks het volgen van therapie is de terugval erg hoog bij elk van deze stoornissen (Gloaguen, Cottraux, Cucherat, & Blackburn, 1998; Silverman, DeFulio, & Sigurdsson, 2012). Eén van de mogelijke oorzaken van zowel de symptomen van deze psychopathologie als de terugval is het verminderd functioneren van het werkgeheugen (Eysenck, 1979, 1982; Eysenck & Calvo, 1992; Silverman, DeFulio, & Sigurdsson, 2012). Dit onderdeel van het geheugen heeft een gelimiteerde capaciteit en is betrokken bij een verscheidenheid aan cognitieve functies, zoals redeneren en leren (Jonides et al., 2008; Miyake & Shah, 1999). Werkgeheugencapaciteit (WGC) wordt dan ook gedefinieerd als de mate waarin doel relevante informatie actief in het werkgeheugen wordt gehouden, ondanks de interferentie van irrelevante informatie (Unsworth & Engle, 2007).

Bij depressieve en angstige personen blijken werkgeheugenprocessen die zorgen voor het inhiberen (Lemelin et al., 1996; Eysenck, Derakshan, Santos, & Calvo, 2007; MacQueen, Tipper, Young, Joffe, & Levitt, 2000; Monsell, 1996; Trichard et al., 1995), het afwenden van hun aandacht van negatieve of angstige informatie (Eysenck et al., 2007; Murphy et al., 1999) en – vooral bij depressieve personen – het updaten van gedachten (Harvey et al., 2004; Joormann & Gotlib, 2008; Whitmer & Banich, 2007) minder goed te functioneren. Het gevolg van dit disfunctioneren is dat negatieve of angstige informatie in het werkgeheugen blijft en zij dus meer moeite hebben om van hun negatieve of angstige gevoelens af te komen dan gezonde personen (Bishop, 2009; Nolen-Hoeksema, 2000).

De werkgeheugencapaciteit vermindering die bij verslaafden is gevonden (Ambrose, Bowden, & Whelan, 2001; Bolla, Brown, Eldreth, Tate, & Cadet, 2002; Jovanovski, Erb, & Zakzanis, 2005) wordt geassocieerd met gedrag wat veel voorkomt bij deze groep. Deze associatie betreft verminderde beslisvaardigheden (Noël, Bechara, Dan, Hanak, & Verbanck, 2007), een sterke aandachts*bias* voor middelen gerelateerde stimuli (Field & Cox 2008; Franken, 2003), een hoog niveau van impulsiviteit (zie voor een review De Wit, 2009) en *delay discounting* (Bobova, Finn, Rickert, & Lucas, 2009; Shamosh et al., 2008). *Delay discounting* is de voorkeur voor snelle kleine beloning in plaats van een uitgestelde grotere beloning, hetgeen meer wordt waargenomen bij verslaafde personen dan bij niet-verslaafde personen.

Recentelijk onderzoek suggereert dat het mogelijk zou zijn om WGC te verhogen (Chein & Morrison, 2010; Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Morrison & Chein, 2011). Deze WGC vergroting lijkt bovendien te kunnen leiden tot klinisch relevante verbeteringen in verscheidene doelgroepen die lijden onder cognitieve problemen, zoals personen met ADHD (Klingberg, Forssberg, & Westerberg, 2002; Klingberg et al., 2005), schizofrenie (Subramaniam et al., 2012) en mensen die herstellen van een beroerte (Åkerlund, Esbjörnsson, Sunnerhagen, & Björkdahl, 2013; Westerberg et al., 2007). Ook bij gezonde studenten bleek werkgeheugentraining een positief effect te hebben: een training met een emotionele component resulteerde in verbeterde emotieregulatie (Schweizer, Grahn, Hampshire, Mobb, & Dalgleish, 2013). Op het gebied van verslaving laten de studies van Bickel, Yi, Landes, Hill en Baxter (2011) en Houben, Wiers en Jansen (2011) zien dat het trainen van het werkgeheugen respectievelijk kan leiden tot verminderde *delay discounting* en tot minder alcoholinname.

Andere studies laten echter geen effect zien van training op het werkgeheugen en gerelateerde factoren zoals ruminatie en intelligentie (Onraedt en Koster, 2014; Redick et al., 2013). Desalniettemin lijkt de relatie tussen het werkgeheugen en psychopathologie zo sterk, zijn de resultaten veelbelovend én kan werkgeheugentraining leiden tot een variatie aan mogelijkheden, dat onderzoek naar het effect van werkgeheugentraining bij gezonde, angstige, depressieve en verslaafde personen van toegevoegde waarde is voor zowel de wetenschap als de klinische praktijk. Dit proefschrift onderzoekt dan ook of een training

WGC kan vergroten en kan leiden tot een vermindering van de negatieve consequenties van gebreken in het werkgeheugen. Eerst werd in **hoofdstuk 2** onderzocht of een hoge WGC beschermt tegen depressieve gevoelens en een negatieve interpretatie *bias*. In de **hoofdstukken 3 tot en met 7** werd vervolgens het effect van werkgeheugentraining op WGC, psychopathologie, welzijn, academische prestatie en gerelateerde factoren bekeken.

Bevindingen

In **hoofdstuk 2** bekeken we of een hoge WGC beschermt tegen depressieve gevoelens en een negatieve interpretatie bias. We onderzochten dit door studenten met een hoge en studenten met een lage WGC willekeurig te verdelen over taken die het WG belastten en taken die het bijna niet belastten. Vervolgens kregen ze een stemmingsinductie om een droevige stemming op te roepen. Hierdoor konden we nagaan of het belasten van het werkgeheugen eerder zou leiden tot negatieve gedachten, een negatieve interpretatie *bias* en moeite met het ophalen van autobiografische specifieke herinneringen bij studenten met een lage WGC in vergelijking met de andere drie groepen. Deze verwachting kwam niet uit de resultaten. We zagen echter wel dat een hoge werkgeheugenbelasting, onafhankelijk van iemand zijn WGC, resulteerde in meer angst en een vermindering van blijdschap, vergeleken met een lage belasting. De resultaten lijken te suggereren dat de grootte het WGC geen invloed heeft op het kunnen omgaan met negatieve gedachten, maar dat het belasten van het werkgeheugen wel leidt tot meer negativiteit.

Bij de studies beschreven in **hoofdstukken 3 tot en met 7** onderzochten we het effect van een werkgeheugentraining. Dit deden we door een belastende werkgeheugentraining - die (behalve in **hoofdstuk 3**) zich aanpaste aan de WGC van de deelnemer - te vergelijken (experimentele groep) met een placebo training die het werkgeheugen minimaal belastte (placebo groep). Meer specifiek werd in **hoofdstuk 3** het effect van een werkgeheugentraining onderzocht op WGC, depressie, angst en ruminatie bij mensen die leden aan een depressie of angststoornis. De training leidde enkel tot een vermindering van angstsymptomen bij depressieve personen. Daarnaast bleek dat een hoger niveau van angst vóór de training voorspellend was voor een grotere vermindering van angst door de training. Verder werd er geen effect van de belastende training

gevonden op ruminatie, depressie of WGC. Beide groepen, dus onafhankelijk van de mate van belasting van het werkgeheugen, hadden een vergrote WGC en minder angstsymptomen na de training in vergelijking met voor de training. De depressieve personen ondervonden ook een vermindering van hun depressie en ruminatie gedurende het onderzoek.

In **hoofdstuk 4** werd dezelfde onderzoeksvraag als in **hoofdstuk 3** onderzocht maar met andere trainingstaken en een zwaardere intensiteit. Ook in deze studie bleek WGC niet te zijn vergroot door een werkgeheugentraining en werd er tevens geen effect gevonden op de mate van ruminatie, angst en depressie. Hetzelfde patroon met betrekking tot de verandering van WGC en symptomen over tijd werd gevonden als in **hoofdstuk 3**. De WGC vergrootte en de symptomen verminderden in beide groepen.

In **hoofdstuk 5** werd dezelfde training gebruikt als in **hoofdstuk 4** maar nu bij personen die opgenomen waren in voor een verslaving aan alcohol, cannabis of cocaïne. We onderzochten of het trainen van het werkgeheugen leidde tot een vergrote WGC en een vermindering van inname en drang naar middelen, impulsiviteit, aandachts*bias* voor middelen, angst en depressie. Beide groepen verbeterden op de getrainde taken maar dit leidde niet tot een grotere WGC voor de experimentele groep. Ook werd op geen enkele van de gemeten maten een effect van de werkgeheugentraining gevonden. Bij beide groepen vonden we een vermindering van gebruik, drang naar middelen, impulsiviteit, depressie en angst. Aangezien beide groepen in therapie waren zou deze verbetering hierdoor kunnen zijn veroorzaakt.

Hoofdstuk 6 richtte zich op het trainen van gezonde studenten. We verwachtten dat het volgen van twee weken werkgeheugentraining zou leiden tot een verbetering van het werkgeheugen, studie prestatie, *coping*, zelf- en aandacht controle en een vermindering van stress, impulsiviteit, intrusies en angst en depressie symptomen. Ook in deze studie werd geen effect van werkgeheugentraining gevonden op WGC of de meegenomen maten. Onafhankelijk van de soort training werden studenten meer relaxed en vrolijk, minder somber, angstig en gestreststst, rumineerden ze minder en hadden ze minder intrusieve gedachten. Daarnaast veranderde hun *coping* stijl. De resultaten op de

werkgeheugentaken waren inconsistent, wat aanduidt dat het niet duidelijk was of hun WGC was vergroot. Tegen de verwachting in was het aantal gevolgde trainingen niet méér voorspellend voor de vermindering van drang naar middelen of de verandering in WGC in de experimentele groep dan in de placebo groep.

In de studie beschreven in **hoofdstuk 7** werd bekeken of een zogenaamde *gegamificeerde* werkgeheugentraining zou leiden tot een vergrote WGC en minder depressie, angst en ruminatie in dysfore studenten. Daarnaast vergeleken we hun WGC en hun klachten voor en na de training met die van gezonde studenten. Naar verwachting waren de klachten van de dysfore studenten ernstiger dan die van hun gezonde medestudenten. Opmerkelijk verschilden ze echter niet in WGC. Betreffende de werkgeheugentraining, resulteerde de experimentele training in een grotere WGC dan de placebo training en zelfs in een grotere WGC dan dat van de gezonde studenten. Helaas had deze verbetering van het werkgeheugen geen effect op de klachten van depressie, angst en ruminatie; verschil in psychopathologie tussen de dysfore en gezonde studenten bleef dan ook bestaan. Bij zowel de experimentele als de placebo groep verminderden de klachten wel over tijd. Onverwacht was dat het aantal gevolgde trainingen niet méér voorspellend was voor enige verandering in psychopathologie of WGC in de experimentele groep dan in de placebo groep.

Conclusie

Dit proefschrift leidt tot een aantal waardevolle conclusies voor zowel wetenschap als praktijk. Hier worden de belangrijkste conclusies genoemd. Het effect van werkgeheugentraining op de WGC is inconsistent en leidde daarnaast in geen enkele studie tot verminderde depressie klachten of ruminatie. Bij verslaafde personen resulteerde de training ook niet tot een vermindering van middelengebruik, drang naar middelen, aandachtsbias voor middel gerelateerde stimuli en impulsiviteit. Gezonde studenten profiteerden ook niet van een werkgeheugentraining op het gebied van studieprestatie, coping, zelf- en aandacht controle, stress, impulsiviteit en intrusies. Interessant is dat een hoger niveau van angstklachten vóór de training voorspellend bleek voor een grotere vermindering van angstklachten bij mensen met een angststoornis of depressie.

Een aantal limitaties van de beschreven onderzoeken zijn de hoge uitval van deelnemers gedurende het onderzoek, de variatie aan medicatie gebruik waarvoor niet geheel gecorrigeerd kon worden en de korte trainingsduur. Daarnaast lijken onze deelnemers ouder en hoger opgeleid, waren er meer mensen van Nederlandse etniciteit en hadden ze ernstigere klachten in vergelijking met mensen die lijden aan deze stoornissen gebaseerd op bevolkingsonderzoeken (e.g. Beck, Steer, & Brown, 1996; Butler, Fennell, Robson, & Gelder, 1991; Centraal Bureau voor de Statistiek, 2013; De Graaf, Ten Have, & Van Dorsselaer, 2010).

Het doel van dit proefschrift was meer inzicht te geven in de effectiviteit van een werkgeheugentraining voor verschillende doelgroepen. Met onze meetmethodes en studie opzet lijkt werkgeheugentraining niet te slagen voor het verminderen van depressie klachten, ruminatie, van middelengebruik, drang naar middelen, aandachtsbias voor middel gerelateerde stimuli, intrusies, stress en impulsiviteit of verbetering van studie prestatie, coping en zelf- en aandacht controle. Deze bevindingen komen overeen met een aantal kritische reviews (Melby-Lervåg & Hulme; Shipstead, Redick, & Engle, 2012) en empirische studies (Onraedt & Koster, 2014; Redick et al., 2013). Ondanks dat werkgeheugentraining tot veelbelovende mogelijkheden zou kunnen leiden, laten de resultaten van dit proefschrift zien dat gebruik van deze nieuwe therapiebenadering kritisch moet worden beschouwd.

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Curriculum Vitae and Publications

Curriculum Vitae

Sabine Wanmaker was born on January 20th 1987, in Rotterdam, the Netherlands. She completed her secondary school at Gymnasium Juvenaat in Bergen op Zoom and started her Bachelor Psychology at the Erasmus University Rotterdam in 2005. Sabine followed extra Psychology courses on the Universidad Complutense Madrid. She worked as student assistant for Dr. Elke Geraerts during her studies. After her Masters she followed the Advanced Research Program and started in February 2011 her PhD research under supervision of Dr. Geraerts and Professor Franken, which resulted in this dissertation. As a PhD student Sabine engaged in setting up and teaching the Master's course Forensic Psychology and supervised research projects of Bachelor and Master students. Furthermore, she co-organized the international SARMAC conference and joined several other committees at the department of Psychology.

Publications

De Graaf, B., van der Heide, L., Wanmaker, S., & Weggemans, D. (2013). The Anders Behring Breivik trial: Performing justice, defending democracy. ICCT research paper.

Moors, A., De Houwer, J., Hermans, D., Wanmaker, S., van Schie, K., van Harmelen, A., De Schrijver, M., De Winne, J., & Brysbaert, M. (2012). Norms of valence, arousal, dominance, and age of acquisition for 4300 Dutch words. *Behavior Research Methods, 45,* 169-177.

Wanmaker, S. (2011). Depressie ontregeld. *De Psycholoog, 5*, 50-53.

Wanmaker, S. (2012). Op de digitale divan. *De Psycholoog, 6*, 24-25.

Wanmaker, S., Geraerts, E., & Franken, I.H.A. (in press). A working memory training to decrease rumination in depressed and anxious individuals: A double-blind randomized controlled trial. *Journal of Affective Disorders.*

Submitted manuscripts

Geraerts, E., Wanmaker, S., Weinstock, E., & Mayer, B. *First, do no harm: the influence of recovered memory therapy on psychopathology*. Manuscript submitted for publication.

Hopstaken, J.F., Wanmaker, S., van der Linden, D., & Bakker, A. Do Dysphoric Thoughts Lead to Divergent Mental Fatigue Effects on a Cognitive Task? Manuscript submitted for publication.

Van Schie, K., Wanmaker, S., Yocarini, I.E., & Bouwmeester, S. *Psychometric qualities of the thought suppression inventory-revised in different age groups.* Manuscript submitted for publication.

Wanmaker, S., Geraerts, E., & Franken, I.H.A. *Training students' working memory to improve academic performance and psychological well-being.* Manuscript submitted for publication.

Wanmaker, S., Geraerts, E., van den Berg, L., Mayer, B., & Franken, I.H.A. *Pushing working memory to the limit - the influence of cognitive load on mood.* Manuscript submitted for publication.

Wanmaker, S., Geraerts, E., van den Berg, L., Mayer, B., & Koster, E. *Effects of working memory training in depressive and anxious patients.* Manuscript submitted for publication.

Wanmaker, S., Geraerts, E., van de Wetering, B.J.M., Renkema, P.J., & Franken, I.H.A. *A randomized double-blind placebo-controlled clinical trial of the efficacy of working memory training in substance use patients.* Manuscript submitted for publication.

Wanmaker, S., Hopstaken, J.F., Asselbergs, J., Geraerts, E., & Franken, I.H.A. *Decreasing dysphoric thoughts by a working memory training: a randomized double-blind placebo-controlled trial.* Manuscript submitted for publication.

Academic conference presentations

Wanmaker, S., Geraerts, E., Franken, I.H.A., Mayer, B., & van den Berg, L. (2014, July). *Tackling depression and anxiety by training working memory.* Paper presentation at International Congress of Cognitive Psychotherapy, Hong Kong, China.

Wanmaker, S., Geraerts, E., & Franken, I.H.A. (2014, January). *Does working memory training work in psychopathology?* Presentation at Experimental Psychopathology Symposium, Heeze, the Netherlands.

Wanmaker, S., Geraerts, E., & Franken, I.H.A. (2013, July). *Tackling depression: A working memory intervention.* Paper presentation at World Congress of Behavioural and Cognitive Therapies, Lima, Peru.

Wanmaker, S., Geraerts, E., & Franken, I.H.A. (2012, November). *Psychopathologie aanpakken met een werkgeheugen training.* Paper presentation at Vereniging voor Gedragstherapie en Cognitieve Therapie congres, Veldhoven, Nederland.

Wanmaker, S., Geraerts, E., & Dijkstra, K. (2012, July). *False memories in recovered memory therapy: Causes and consequences.* Paper presentation at International Congress of Psychology, Cape Town, South Africa.

Wanmaker, S., Geraerts, E., van den Berg, L., Mayer, B., & Koster, E. (2011, September). *Working memory deficits underlying depression and anxiety.* Paper presentation at Graduate

Research Day of the institute of Psychology at Erasmus University, Rotterdam, the Netherlands.

Wanmaker, S., Geraerts, E., & Dijkstra, K. (2011, June). *False memories in recovered memory therapy: Causes and consequences.* Paper presentation at Society of Applied Research in Memory and Cognition, New York, United States.

Poster presentations

Wanmaker, S., Geraerts, E., & Franken, I.H.A. *A working memory training as a new intervention ror depression and anxiety.* Poster presentation at Graduate Research Day of the institute of Psychology at Erasmus University, Rotterdam, the Netherlands.

Wanmaker, S., Geraerts, E., & Dijkstra, K., (2013, May). *Memory distortions in people recovering memories of previous lives.* Poster presentation at Association for Psychological Science annual convention, Washington, United States.

Wanmaker, S., Geraerts, E., van den Berg, L., Mayer, B., & Koster, E. (2011, September). *Working memory deficits underlying depression.* Poster presentation at European Association for Behavioural and Cognitive Therapies, Reykjavik, Iceland.