Tackling depressive disorder and anxiety: A working memory intervention as addition to treatment as usual

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Study whether a working memory training as addition to treatment as usual decreases the depression and anxiety complaints.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON39689

Source
ToetsingOnline

Brief title
A working memory intervention

Condition

- Other condition

Synonym
anxiety disorder , Major depressive disorder/depression

Health condition

Zowel depressie als angststoornissen

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus Universiteit Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Anxiety, Depression, Treatment, Working memory

Outcome measures

Primary outcome

- Scores on questionnaires:

BDI-II: depression

RRS: rumination

STAI: anxiety

- Scores on other measures that have a link with depression and anxiety:

AMT: specificity of the autobiographical memory

- Scores on working memory tasks:

N-back task

Symmetry Span

Internal Shift Task

Reading Span

Digit Span

- Score on diagnostic interview:

SCID-I: depression and anxiety

Secondary outcome

Not applicable.

Study description

Background summary

First we will tell you about depression, then we will focus on anxiety and finally both disorders will be linked in the part about working memory training:

Depression:
The life of individuals with a depressive disorder changes significantly. A depression changes the way people feel and how they perceive themselves as well as the world around them. According to the World Health Organisation (WHO), around 12% of the population is suffering from clinical depression, making it among the most prevalent psychiatric disorders. The WHO estimates that this number is increasing, and that by the year 2020, depression will be the most prevalent disorder causing disability for all ages in men and women. In addition to the distress depression causes to individuals and their families, this emotional disorder also incurs extensively direct and indirect economic costs, which for instance in the Netherlands exceeds one billion Euros annually and in the United States of America 65 billion dollars. Clearly, more research is needed to increase the understanding of the causes and maintenance of this disorder, and to enhance prevention and treatment. Therefore the current proposal is aimed at examining crucial underpinnings of depression and also aspires to yield a novel approach of clinical treatment by targeting these deficits. Apart from important neurobiological research examining the onset and maintenance of depression, a dominant focus in the past 30 years has been on cognitive models of depression. These posit that selective information processing plays a crucial role in the development and maintenance of this disorder (for a review, see Williams, Watts, MacLeod, & Mathews, 1988, 1997). That is, how people think, make inferences, approach certain situations, attend to certain events, and how they recall these events determine their emotional responses and, as a consequence, whether or not they are likely to incur a depression. Clearly, cognitive processes play a crucial role in how much people are affected by negative experiences and determine whether these events will be followed by quick recovery or by recurring depressive episodes. These models, therefore, make the important assumption that investigating the content of cognition and the nature of cognitive processes in depression is essential for our understanding of the onset and maintenance of this disorder. The extensive research programs generated by these cognitive models have shown that depressed individuals are characterised by preferential processing of negative material, difficulties in disengaging attention from negative information, interpreting

ambiguous information in a negative way and recalling events in a more negative and more general fashion than they originally were (Mathews & MacLeod, 2005). Recently, new procedures (i.e., cognitive bias modification; CBM) have been developed and studied to manipulate these biases and the first steps have now been made to experimentally employ these CBM procedures for improving cognitive deficits in depression. For instance, Watkins, Baeyens, and Read (2009) administered a concreteness training that successfully overcame the depression-related cognitive bias to process self-relevant information in an overgeneralised manner. In a similar vein, Holmes and colleagues demonstrated that modifying maladaptive interpretations reduces depressive intrusions (e.g., Holmes, Lang, & Shah, 2009). An important concept in understanding these dysfunctional cognitive processes is working memory. Working memory is commonly described as a system for the active maintenance and manipulation of information in memory and for the control of attention (Baddeley & Hitch, 1974). The capacity of this system is limited; therefore it is important that its contents are updated efficiently, which is controlled by executive processes (e.g., Friedman & Miyake, 2004). Executive processes direct the access to working memory, by removing information that is no longer relevant, as well as protecting it from intrusions. If these processes perform poorly, cognitive and emotional functioning are likely to be affected. For example, poor interference resolution may lead to more intrusive thoughts. In fact, increased interference from irr

elevant intrusions has been suggested as a source of low working memory capacity (Geraerts, Merckelbach, Jelicic, & Habets, 2007). Irrelevant negative intrusions are an important characteristic of depression. Indeed, such deficient executive functioning has been linked to depression (Joormann, 2010). Emerging evidence now shows that depression is characterized by difficulties in the inhibition of mood-congruent material, resulting in prolonged processing of negative, goal-irrelevant aspects of presented information. This in turn hinders recovery from negative mood and leads to sustained negative affect, which is typical for depressive episodes. Accordingly, theorists have suggested that deficits in executive functioning lie at the heart of biases in attention, interpretation, and memory in depression. They are said to lead to ruminative responses to negative events and, consequently, negative mood states. Indeed, a study by Joormann and Gotlib (2008) has shown that interference control was decreased in depressive patients. This means that they experienced difficulty from removing irrelevant material from working memory. Noticeably, this increased interference was linked to rumination, one of the hallmark symptoms of depression. This association was still evident after a 6-month period (Zetsche & Joormann, in press). Similarly, Goeleven, de Raedt, Baert, and Koster (2006) found that depressed patients showed strongly impaired inhibition of negative affect. These findings of executive deficits in depression have been backed up by neuroscientific work, which indicated abnormalities in neural function underlying difficulties in inhibition of negative thoughts in depressed individuals (Koster, De Lissnyder, Derakshan, & De Raedt, in press). One wonders whether such executive deficits can be trained in the same manner as those deficits targeted in cognitive bias modification procedures. Is it possible to improve executive processes, which then in turn influence higher-order cognitive abilities and even overt behaviour?

Anxiety:
An anxiety disorder consists of an ongoing and severe kind of anxiety without the presence of a realistic threat. There are
different kinds of anxiety disorders, for example panic disorders, agoraphobia, social phobia, generalized anxiety disorders
(GAD) and obsessive compulsive disorders (OCD). Together with mood disorders and substance use disorders, anxiety
disorders are among the most prevalent mental disorders (Brysbaert, 2006). The World Health Organisation (WHO; 2010)
estimates that around 12% of the population suffers from clinical anxiety every year. The life of people with an anxiety disorder
changes significantly. Symptoms of anxiety are frequently associated with a variety of physical symptoms like sweating, heart
palpitations and trembling. Anxiety causes a great deal of distress to the patients and to their families. In addition, anxiety
disorders cause significant economic costs. For example, these disorders were costing the Netherlands 285,6 million euros in
2005 (Van Wieren, Schoemaker, & Van Balkom, 2010). Treatment strategies for anxiety disorders include cognitive therapy,

cognitive-behavioral therapy, psychopharmacology, exposure therapy, relaxation training, biofeedback, meditation, supportive psychotherapy, psychodynamic psychotherapy, and other forms of psychotherapy (Miller, Fletcher, & Kabat-Zinn, 1995). The most common treatment strategies these days are cognitive-behavioral therapy and psychopharmacology. Past research indicates that both genetics and important events in a person*s life are playing a significant role in the development of anxiety disorders. However, because there is still a lot unknown about the aetiology and maintenance of these disorders, more research is needed to address these issues and to enhance prevention and treatment. Therefore the current proposal aims to examine important cognitive processes involved in anxiety and aspires to set up a new approach to a clinical treatment method targeting these processes.

Over the past three decades cognitive models of anxiety disorders have demonstrated that selective information processing plays an important role in the development and maintenance of anxiety (Williams, Watts, MacLeod, & Mattews, 1988). More specifically, recent studies provide considerable evidence to state that anxiety is strongly associated with an attentional bias towards threatening stimuli and biases in interpretation and memory (Mathews & MacLeod, 1994; Mathews & MacLeod, 2005).

Patients with an anxiety disorder tend to interpret ambiguous information in a negative way. Several researches demonstrate that individuals reporting high levels of anxiety display a disproportionate ability to identify or detect emotionally negative words (e.g. Foa & McNally 1986; as described in Mathews & MacLeod, 1994). For example, during Stroop tasks, anxious individuals display problems ignoring the emotionally negative content of threat-related stimulus words (e.g. Mathews & MacLeod 1985; as described in Mathews & MacLeod, 1994). However, the nature of the relation between anxiety and cognition is far from clear. Therefore, it is necessary to get more insight in the cognitive processes behind anxiety.

A lot of past research shows that high levels of anxiety are associated with a reduced ability to perform complex cognitive tasks (Mueller 1992, Watts & Cooper 1989; as described in Mathews & MacLeod, 1994). A lot of researchers state that these reductions are being caused by a depletion of capacity-limited cognitive resources, especially working memory (Eysenck & Calvo 1992, Ellis & Ashbrook 1988; as described in Mathews & MacLeod, 1994). Therefore, working memory is an important concept in understanding the cognitive biases associated with anxiety disorders.

Working memory can be described as a limited capacity system for the temporary, active maintenance and storage of information (Baddeley, 2003). This system is critical for human

thought processes. The ability to retain and manipulate information in working memory is linked with the prefrontal cortex (Fuster, 1989; Goldman-Rakic, 1987; as described in Klingberg, Forssberg, & Westerberg, 2002) and underlies different executive functions, such as problem solving and reasoning (Engle, Kane, & Tuholski, 1999; Hulme & Roodenrys, 1995; Klingberg, 2000; as described in Klingberg et al., 2002). The theoretical concept of working memory argues that working memory is important for human thought processes because it provides an interface between perception, long-term memory and action (Andrade, 2001; Miyake & Shah, 1999; Conway, Jarrold, Kane, Miyake, & Towse, 2007; as described in Klingberg et al., 2002). Reduced working memory capacity is associated with several neurological and psychiatric disorders like schizophrenia and ADHD (Goldman-Rakic, 1994; Castellanos & Tannock, 2002; as described in McNab et al., 2009).

Working memory training:
Seminal work by Klingberg and colleagues has demonstrated that training the working memory is possible. These researchers showed that training of working memory in both children and adults improved their executive functioning and higher-order abilities such as reasoning (Klingberg, Forssberg, & Westerberg, 2002). This improvement was related with changes in cortical activity (McNab et al., 2009). Interestingly, in a sample of children with attention deficit/hyperactivity disorder (ADHD) a working memory training improved executive functioning but also led to a significant reduction in the severity of ADHD symptoms (Klingberg et al., 2005). Likewise, Jaeggi, Buschkuehl, Jonides, and Perriq (2008) showed that a working memory training improved participants* reasoning and problem solving skills. Recent studies showed that even in schizophrenia (Subramaniam et al., 2012) and in people with alcohol problems (Houben, Nederkoorn, Wiers & Jansen, 2011) the complaints decreased after training the working memory. Noticeably, these different lines of research all point towards one conclusion: individual differences in the ability to control the contents of working memory may be related to the onset and maintenance of depressive disorder. Improving working memory abilities could therefore tackle what may be at the root of depression.

Results from previous studies from our research team (not yet published) showed that people who already did cognitive behavioral therapy showed the best improvement when executing a working memory training. Cognitive behavioral therapy has good results but this can be increased when combined with another therapy. We also aim to increase the effectivity of the other treaments of PsyQ for anxiety and depression complaints. As all therapies share the cognitive component with cognitive behavioural therapy we think the change is high that the addition of a working memory training will indeed increase the effecitivty.

Study objective

Study whether a working memory training as addition to treatment as usual decreases the depression and anxiety complaints.

Study design

128 patients in double blind RCT in two groups: working memory training or a bogus working memory training as addition to their treatment as usual.

Pre-test:
• SCID-I: depression and anxiety modules
• BDI-II: depression
• RRS: Rumination (standard, frequently used test for measuring rumination)
• STAI: anxiety state and trait
• AMT: Autobiographical Memory Test (standard, frequently used to test the specificity of autobiographical memory)

Working memory training (and half of the patients bogus training):
4 weeks, six times a week 25 minutes on the computer
N-back task and symmetry span task: both reliable, valid and often used working memory tasks. The tasks in the working memory training condition will be adapted to the level of the patient to train the working memory. Because of the adaption it is never too hard or easy for the patient. The same tasks will be executed in the bogus training, but the level will not adapt and will stay at a really easy level. The training can be executed via a website whenever and where the patient like to do it.

Post-test (after 4 weeks):
• SCID-I: depression and anxiety modules
• BDI-II: depression
• RRS: Rumination (standard, frequently used test for measuring rumination)
• STAI: anxiety state and trait
• AMT: Autobiographical Memory Test (standard, frequently used to test the specificity of autobiographical memory)

Intervention

Trainingtasks which have to be executed by the patient six times a week for 4 weeks:

- Symmetry Span Task: The symmetry span task consists of images, presented on a computer screen, that have to be judged by the participant on symmetry. After the judgment a stimulus will be presented (a red square in a grid of 4x4), from which the participant has to remember the location. The participant get the possibility to practice the judgment of symmetry in 15 pictures. After that, they practice the square part (2 times 2 squares and 2 times 3 squares).

As last practice phase they can practice the combination of these two parts (3 times 2 symmetry pictures and squares). The experiment consists of 17 trials in which the participant has to remember 2 to 17 squares, they start with 2 squares. If they remember the squares correctly and judge the symmetry pictures correctly as well, the level will increase (3 squares). When they make a mistake on one or both parts they will stay on the same level. The computer programme randomly pick the pictures and squares. The symmetry span is a task in the same category as the reading- or digit span and is a good method to train the working memory.

The symmetry span is the same for the control group, however they stay on the same level with only 2 symmetry pictures and squares. Because the task is easy and does not adapt, the working memory will not be trained.

- N-back task:

In the N-back task the participant sees a black computer screen with a white cross. On the screen a blue square can light up in 8 different positions. The participant sees the square for 1 second and on the same time a letter will be heard (letters: F, H, C, L, K, Q, S, T). The location of the square and the letter has to be remembered by the participant. On every presentation the square and letter has to be compared with the square and letter a certain steps before. The subject presses the a-key if the square is the same, the l-key if the letter is the same, and both keys if both stimuli are the same. The subject get a visual instruction before starting the real experiment. They begin with the 1-back task where they have to compare the letter and square with the stimuli 1 step back. The pre- and post task consists of 10 trials. If the subject makes less than 3 errors on the trial (in both parts) the level will increase with one; the distance between the to remember stimuli and showed stimuli will get bigger (1-back, 2 back, maximum of 5-back). If they make more than 5 errors they will go to a lower level. The training consists of 13 trials. The computer randomly generate the squares and letters. The N-back task is a frequently used test for training the working memory and studying it (Jeaggi, Studer-Luethi, Buschkeuhl, Su, Jonides & Perrig; 2010). Tje control group does the same task but they execute the 0-back; they have to compare the present stimuli with the first stimuli. Because the task is easy and does not adapt to the level of the subject, the working memory is not trained.

Study burden and risks

The task will cost the participant one and a half hour at the pre- and post-test and weeks 6 times a week 25 minutes. They can execute the training whenever and where they want. There are no risks linked with this study.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Suffering a major depressive disorder and/or anxiety disorder (except a specific phobia)
Waiting on a waitinglist of PsyQ
Age between 18 and 67
Speaking fluently Dutch
First episode op depression or therapy for anxiety

Exclusion criteria

- Suffering a bipolar disorder
- Suffering exclusively a specific phobia
- Suffering from psychotic complaints

- Drugs or alcohol dependence

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-02-2013
Enrollment:	128
Type:	Actual

Ethics review

Approved WMO Date:	15-02-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-05-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL42685.078.12