

Decreasing Dysphoric Thoughts by a Working Memory Training: A Randomized Double-Blind Placebo-Controlled Trial

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Abstract

Objective: Depressive symptoms are related to deficient executive functioning, in particular working memory (WM). That is, depressed individuals are less able to remove negative information from their WM, have difficulties to shift between negative and positive information and inhibit irrelevant information. Previous findings show that working memory capacity (WMC) can be increased by training and this diminishes symptoms of psychopathology, like ADHD, and cognitive consequences of a stroke. The inclusion of game elements in a WM training showed to positively influence motivation, compliance and WM performance during and after training. The current study aimed to explore the effectiveness of a gamified WM training for dysphoria.

Method: 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. Participants executed the game, consisting of five WM tasks, three times a week for three weeks at home. The experimental group the tests adapted to their WMC level, to train their WMC, while the placebo group received easy versions of the tasks to prevent training WMC. Before and after the training participants' WMC was assessed with the Spanboard Task and their psychopathology with questionnaires about depression, anxiety, and rumination. Moreover, WMC and psychopathology were compared to a healthy control group before training.

Results: As expected, the dysphoric students reported more psychopathology than the healthy students. The groups did not differ in WMC. WM training resulted in a larger WMC compared to the placebo training and compared to healthy students, but not in a larger decrease of psychopathological symptoms. However, both WM and placebo training resulted in a less reported psychopathology. The number of training sessions did not moderate the effect of training on either measure.

Conclusion: A gamified WM training seems to increase WMC but this did not transfer to a decrease of psychopathology. A potential explanation for this lack of effect might be that participants' psychopathology was not severe enough to tackle it with a WM training. Another suggestion might be that WM training is not as effective for depression, anxiety and rumination, which is in line with other recent studies.

Keywords Working memory; Depression; Anxiety; Rumination; Working memory training; Dysphoria; Executive functioning

Introduction

Depression negatively affects health [1,2], personal relationships[3], and productivity [4]. In students depression is associated with lower educational performance [3,5,6] and higher drop-out rates from education [7,8]. Especially ruminating about a dysphoric mood is associated with difficulties in concentration [9], complex problem solving [9-10], and impaired work strategies [9]. 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. [11,12].

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. [13]. Several separable key processes support efficient functioning of WM [14-16]. Depressive individuals show impairment in these processes. Particularly, depression results in an impaired ability to remove negative information from WM once it has entered [17-19]. In addition, depressive individuals have difficulties in shifting between negative and positive information [20,21], which manifests in a bias for negative information [22]. Furthermore, their ability to inhibit irrelevant information is reduced [23-26]. Depression symptoms, like difficulties in learning [27-29], attention [28-30], concentration [29], decision-making [31] and planning [30,32-33] are expressions of WM deficits as WM controls all these functions. A study of Owens, Stevenson, Hadwin, and Norgate [34] 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 [35-39]. Critics, on the other hand, indicate that results regarding generalization of WM training to other skills are mixed [40-42]. 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 [43]. Owens, Koster, and Derakshan [12] 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 [44] 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 [42]. This can be reached by using a level that is neither boring nor too challenging [42] and by the addition of game elements [45]. For instance, Prins and colleagues [45] 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 [11,46,47]. 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, Buschkuhl, Jonides, and Perrig [48] 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 moderated by 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 (Figure 1). The inclusion criterion was a Beck Depression Inventory [49] 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 ($\chi^2(2)=.04, p>.05$), students with a Dutch nationality ($\chi^2(2)=.43, p>.05$), 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 (Table 1; $\chi^2(1)=3.36, p>.05$), history of therapy ($\chi^2(1)=.09, p>.05$) and use of medication for their psychopathological complaints ($\chi^2(1)=.60, p>.05$).

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

Table 1: Demographic Variables

Measures

Working memory

Spanboard Task. WM performance was measured using a computerized version of the Spanboard task adapted from Prins et al. [45]. The user is shown a 4x4 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 [49]; Dutch version [50] 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 [51], with a Cronbach's α of .94 in the present study.

Anxiety: The State-Trait Anxiety Inventory (STAI) [52]; Dutch version [53] 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 [54], with a Cronbach's α of .97 in the state part and .96 in the trait part in this study.

RuminationL: The Ruminative Response Scale (RRS [55]; Dutch version [56]) 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 [57], 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. [58]. 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 have 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 [59] First, users see an 8x8 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 [60], 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 4x3 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. [61,62]. 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 (Tables 2 and 3). However, this increased capacity did not lead to a larger improvement of psychopathological complaints (Tables 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 (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 (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 (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 ($U=25.50, z=-5.30, p<.01, r=-.77$).

	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 2: Mean and Standard Deviations of Working Memory and Psychopathology Measures per Group

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
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Table 3: Effect of Working Memory Training on Working Memory and Psychopathology Measures

Regression:

To explore whether the number of completed training sessions moderated the level of change in psychopathology and WMC due to the WM training, we included, besides the standardized predictors, the group*predictor interaction e.g. [63]. The difference scores (pre minus post) of the BDI-II, STAI total, state and trait, the RRS, 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 transferred 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 [64-66]. Cognitive deficits seem to be minimal in young individuals with mild depressive symptoms [64,65], and characterize especially elderly depressed people and severely depressed inpatients with psychotic features [65]. Furthermore, neuropsychological functioning depends on the severity of this disorder e.g. [67-60]. Our sample reported only minor depressive symptoms according to the categorization of Beck and colleagues [49] and compared to some of the other studies that used dysphoric students [12,46]. 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 [70-72] 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 [48,73,74]. Although WMC increased, the transfer

effects on psychopathology were absent. This pattern of results is seen in the study of Owens and colleagues [12] 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. [45,73]. Remarkably, other studies find an effect on far transfer measures, without WMC improvement [48,75-79]. Another category of studies does not find any result on both WMC and far transfer measures e.g. [44,80]. Redick and colleagues [80] aimed to explore the efficacy of WM training using the best and most valid possible method, by taking all preconditions into account [36,42]. 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 [81-83]. 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 [49]. 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 [43], 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 [42]. Performance on tasks can be influenced by numerous factors [80] 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.

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