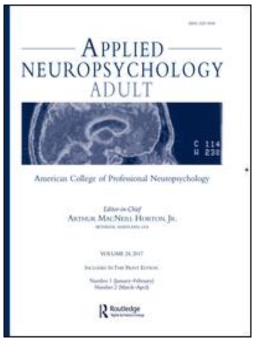

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A pilot study of cognitive remediation in remitted major depressive disorder patients

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ABSTRACT

Major depressive disorder (MDD) is associated with working memory (WM) impairments. These deficits often persist following remission and are associated with rumination, a recognized risk factor for depression relapse. The efficacy of WM-targeted cognitive remediation as a potential relapse prevention tool has not been investigated. The present pilot study aimed to investigate the feasibility, acceptability, and cognitive benefits of a WM-targeted cognitive remediation program in remitted depression. Twenty-eight MDD participants in remission were recruited. The intervention consisted of twenty-five 30–40-minute training sessions, coupled with weekly coaching, administered over a 5-week period. Before and after the intervention, a battery of objective neuropsychological tests and self-report measures was administered. Key outcomes were WM, inhibition and rumination. Acceptability of the intervention was observed, with 83% showing high motivation, along with WM gains for all completers ($n = 18$, 64% of recruited participants). The cognitive remediation selectively improved targeted WM functions, as measured by objective tests. This did not translate into self-reported improvements in everyday WM or inhibition. However, all but one completer achieved at least one personal goal related to WM and 44% achieved two or, the maximum possible, three such goals. For remitters whose WM was significantly enhanced after the intervention, the cognitive remediation also decreased dysphoric-mood related rumination. The successful pilot testing of the WM-targeted intervention supports the conduct of a fully powered randomized controlled trial as a relapse prevention approach in remitted MDD.

KEYWORDS
Cognitive remediation therapy; feasibility; major depression; pilot study; remission; working memory

A pilot study: preventing relapse and recurrence in depression through cognitive remediation in remitted MDD patients

Major depressive disorder (MDD) is the most prevalent mental disorder, with high rates of functional impairment, suicidality, and distress (Otte et al., 2016). Of import, the high risk of recurrence is one of the most debilitating aspects of illness. Half of those diagnosed with a first episode of depression will relapse within two years (Kasper & Eder, 1994; Mueller et al., 1999; Solomon et al., 2000; Stegenga, Kamphuis, King, Nazareth, & Geerlings, 2012; Vittengl, Clark, Dunn, & Jarrett, 2007). The prevention of relapse may be even more difficult than the actual treatment of acute episodes (Figueroa et al., 2015).

Growing evidence indicates that cognitive dysfunction is a core feature of MDD (Marazziti, Consoli, Picchetti, Carlini, & Faravelli, 2010). Specifically, several studies have shown that cognitive functions such as attention, psychomotor speed, executive functions, and memory are affected in depressed individuals (for reviews see: Hammar & Årdal, 2009; Rogers et al., 2004; Ahern & Semkovska, 2017). Whereas cognitive vulnerabilities were traditionally thought to be a state-dependent aftermath of symptoms (Joormann, Yoon, & Zetsche, 2007, Millan et al., 2012; Siegle, Ghinassi, & Thase, 2007), more recent research shows that cognitive deficits remain present after remission (Semkovska et al., 2019), are a risk factor for depression (Koster, Hoorelbeke, Onraedt, Owens, & Derakshan, 2017) and a predictor for relapse (Figueroa et al., 2015; Schmid & Hammar, 2013; Timm et al., 2017).

Cognitive deficits could also interfere with everyday functioning in remission, and leave the individual struggling to meet premorbid levels of functioning. This in turn may enforce negative self-representations, and ultimately increase the risk of relapse (Gotlib & Joormann, 2010; Hammar &

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Årdal, 2009). In line with this, low cognitive function six months after hospital discharge has been linked to poor everyday functioning (Jaeger, Berns, Uzelac, & Davis-Conway, 2006) and persistent unemployment (Baune et al., 2010). Furthermore, subjective reports of difficulties with concentration have been found to relate to decreased role functioning in MDD patients (Buist-Bouwman et al., 2008). Thus, addressing impaired cognitive function once remission is achieved has the potential of decreasing relapse rates and improving everyday function in depression.

One of the cognitive functions adversely affected by MDD is working memory (Christopher & MacDonald, 2005; Prado, Watt, & Crowe, 2018). Working memory deficits persist into remission (Semkovska et al., 2019). Moreover, working memory deficits have been shown to be associated with impaired inhibition (Gohier et al., 2009) and rumination (Joormann, Levens, & Gotlib, 2011), two further risk factors for depression relapse. Cognitive inhibition has been shown to be impaired among those with current and remitted depression (Gotlib & Joormann, 2010). Rumination has also been found to robustly predict the frequency and severity of depressive episodes (Joormann & Gotlib, 2010; Kuehner & Weber, 1999; Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008), relapse to depression (Ronold, Joormann, & Hammar, 2018), and quality of life, social and occupational functioning (Kuehner & Huffziger, 2012).

Impaired working memory might lead to negative information being kept in working memory, consequentially increasing rumination and further leading to subsequent rehearsal of this material which is then stored in long-term memory (Whitmer & Gotlib, 2012). Joormann's model (2006) suggests that depressed individuals are vulnerable to rumination as a result of the inhibitory dysfunction for negative information (see also Joormann, Yoon, & Zetsche, 2007). Specifically, individuals with depression may be biased to attend to and recall negative information, and this is amplified by difficulties in inhibiting such information from working memory. Working memory deficits may thus contribute to greater difficulties with cognitive inhibition and rumination (Zetsche, Bürkner, & Schulze, 2018).

In sum, cognitive deficits have been well-documented in current and remitted depression, have been shown to predict relapse and may help explain other relapse risk factors such as rumination. Although psychological interventions have shown promise in reducing relapse and recurrence (Biesheuvel-Leliefeld et al., 2015), most preventive interventions do not focus on cognitive deficits (Gonda et al., 2015). Thus, the aim of this pilot study is to provide preliminary data regarding a relapse prevention intervention targeting specific cognitive deficits in depression.

Cognitive remediation (CR) are a group of behavioral interventions designed to improve cognitive processes such as attention, memory, and executive function by mobilizing brain plasticity (Semkovska & Ahern, 2017). Primary training of working memory seems to yield generalized cognitive enhancement, including improved cognitive control and fluid intelligence in healthy participants (Morrison & Chein, 2011). The positive effects of CR are well documented in schizophrenia as a way to improve specific cognitive functions and, in combination with psychiatric rehabilitation, to generalize to better functional outcomes (McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007; Wykes, Huddy, Cellard, McGurk, & Czobor, 2011).

Relatively few studies have examined CR in MDD (Porter, Bowie, Jordan, & Malhi, 2013; Porter et al., 2017; Semkovska & Ahern, 2017). In a recent meta-analysis of randomized studies, computerized CR for MDD ($n = 9$) was associated with significant, small to moderate improvements in depressive symptom severity and daily functioning, along with moderate to large improvements in attention, working memory and global cognitive functioning (Motter et al., 2016). More specific interventions designed to address cognitive control have also been shown to reduce risk of depression recurrence (Koster et al., 2017) and brooding rumination (Peckham & Johnson, 2018). Finally, Siegle et al. (2014) randomized trial demonstrated that CR targeting working memory can reduce depressive symptoms and rumination among individuals with current MDD.

Despite these important findings, to the best of our knowledge, the current study is the first to investigate whether CR designed to improve working memory can reduce rumination in formerly depressed participants. The aim of the current study is to evaluate the feasibility and acceptability of a CR program targeting working memory (WM-CR) for patients with MDD in remission. The long-term objective is to evaluate whether CR could address relapse and recurrence in MDD by improving cognitive function and related daily outcomes.

Cogmed Working Memory Training® is an intensive computer-based training tailored to the individual's performance levels. The program also provides personal coaching throughout the training period to prevent attrition. Cogmed has been studied much more frequently than have other commercial working memory training programs (Jaeggi, Buschkuehl, Jonides, & Shah, 2012; Shipstead, Redick, & Engle, 2012). Previous research has shown that Cogmed improves several aspects of cognitive performance (Klingberg, Forssberg, & Westerberg, 2002; Klingberg et al., 2005) and is associated with changes in neural activity (McNab et al., 2009). Nonetheless, Cogmed had not been tested for individuals with remitted depression.

The objective of this pilot study was to evaluate Cogmed working memory training to improved related cognitive deficits, that are WM, inhibition, and rumination, in individuals with remitted MDD and to explore aspects of feasibility. Specific aims were to assess the following:

1. Do people with remitted MDD find WM-CR acceptable and helpful for improving everyday cognitive difficulties associated with working memory efficiency?
2. Do objective and self-report measures of working memory and inhibition show improvement after WM-CR?
3. Are objective cognitive improvements following WM-CR specific to targeted functions (working memory and inhibition) or do they generalize to other non-targeted cognitive functions?

4. Are post-WM-CR cognitive improvements associated with decreased rumination?
5. If any, which baseline characteristics can explain cognitive improvement?

Method

Participants and procedure

The project was approved by the Norwegian Data Inspectorate and The Regional Committee for Medical Research Ethics of Western Norway. The study procedures were consistent with the recommendations of the Helsinki Declaration of the World Medical Association (2009). The present pilot study was conducted at the Neuropsychological Clinic at the Faculty of Psychology, University of Bergen. Participants were recruited from previous depression-related projects, from an outpatient psychiatric clinic in Bergen (Norway), and through advertisements. Inclusion criteria were: previous diagnosis of MDD, for which treatment was received, and currently in remission for at least two previous months, i.e. presenting only minor or no depressive symptoms ($\leq$12 as measured by the Montgomery Åsberg Depression Rating Scale MADRS; Montgomery & Åsberg, 1979). Exclusion criteria were self-reported current substance abuse, or history of neurological disorder (such as brain tumor, cerebral haemorrhage) or organic disease that could interfere with brain functioning.

Individuals who contacted the study team with interest in participating were screened for inclusion- and exclusion criteria through telephone interviews by trained health personnel. Those participants who met the inclusion criteria visited the University for informed consent procedures. Those who provided written informed consent underwent a comprehensive clinical evaluation and then the baseline assessment (T1). All participants met the diagnostic criteria for Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV-TR criteria for MDD (American Psychiatric Association, 2000) at some stage in their life, as assessed using the M.I.N.I. Norwegian version, a structural clinical interview for psychiatric diagnoses in the DSM-IV (Leiknes, Leganger, Malt & Malt, 1999). Within two weeks of T1, participants started the Cogmed WM intervention. Upon intervention completion, a post-treatment (T2) assessment was conducted. At both assessment time points (T1 and T2), a battery of objective neuropsychological tests and self-report measures was administered. Mean completion time was just short of five weeks ($M = 34.78$, SD $= 5.996$, range: 27–50 days). After that subjects were reassessed (T2) after a mean period of roughly three weeks ($M = 22.17$, SD $= 30.137$, range 1–130 days).

Participants received 400 NOK (approximately 49 USD) to cover travel costs and other expenses related to participation.

Cognitive remediation intervention

Cogmed Working Memory (WM) Training is a computer-based CR program designed to enhance WM functions through intensive and systematic training (Pearson, 2016). It consists of verbal and spatial tasks that require attending to multiple stimuli at the same time, holding information in WM during a short delay, as well as sequencing of presented stimuli in a specific order (Bellander et al., 2011). The intervention consists of 25 computer-based sessions, each lasting 30–40 minutes. Training is considered sufficient if at least 20 sessions are completed. In the Cogmed (2016) intervention, difficulty levels are adjusted as a function of individual performance. Cogmed runs on computers or tablets with internet connection which allows participants to complete training at home, school or at work. Participants could borrow a tablet from the project or make use of their own computer or tablet. In the first session, WM exercises required participants to remember only two items, and this number increased with successful performance so that participants would continuously challenge the upper limit of their WM capacity. A coach interacted with participants once a week to provide structure, feedback on progress, and to enhance motivation.

The Cogmed program provides start and progress performance scores allowing the calculation of WM improvement with training (Roche & Johnson, 2014). The Cogmed percent training improvement score was calculated as: (maximum performance score minus start performance score)/start performance score. Subjective motivation was categorized by the program as "low", "average" or "high" based on responses to three motivation questions asked at three time points during the intervention. The program also asked participants to choose three personal goals for the training from a list. After finishing training, participants were asked whether these goals were met or not, which we scored as number of goals met (0–3). For the feasibility analysis, we also considered the frequency and the percentage meeting the goal for each of the goals listed.

Objective outcomes

A trained test technician administered a neuropsychological test battery, which included standardized tests of intellectual function, auditory attention, verbal working memory, verbal long-term memory, and executive function. Unless otherwise specified, raw scores were used in order to achieve a representative distribution as recommended for outcome analyses of pilot studies (Lancaster, Dodd, & Williamson, 2004).

Wechsler abbreviated scale of intelligence

To control for the effect of general intellectual abilities (IQ), the Wechsler's Abbreviated Scale of Intelligence (WASI, Wechsler, 1997) was conducted at T1. This test provides estimates of verbal, performance, and total IQ based on four subtests. WASI is an abbreviated version of the Wechsler Adult Intelligence Scale–III, with demonstrated reliability and validity in the measurement of intellectual functioning (Bosnes, 2009; Hays, Reas, & Shaw, 2002; Ryan et al., 2003). As this was a participant descriptor (rather than outcome) variable, standardized IQ scores were used.

WAIS-III digit span subtest

In the Forward condition of this measure, a sequence of numbers is read aloud to the participant, who is asked to repeat the sequence in the same order. The number sequences get progressively longer, with two trials provided for each specific sequence length. The Digit Span Forward provides an estimate of auditory attention span. In the second condition of the digit span (Backward), the participant is asked to repeat each number sequence in the backward order of that presented. Again, the number sequences get progressively longer. The Digit Span Backward provides an estimate of auditory working memory, as the procedure requires holding and manipulating information in short term memory to re-arrange numbers for production in the requested order (Wechsler, 1997).

D-KEFS color word interference test

The Color-Word Interference Test (CWIT) from the Delis-Kaplan Executive Functioning Scale consists of four subtests that evaluate processing speed, inhibition and mental flexibility (Delis, Kaplan, & Kramer, 2001). The CWIT is premised on the Stroop effect. The two first conditions, Color Naming and Word Reading, yield measures of processing speed/mental efficiency, in which participants are asked in the first condition to label different color ink and in the second condition, to read names of colors written in black ink. In the third condition, measuring inhibition, the color names are written in incongruent ink color. For example, the word "red" might be written in blue ink. The participant has to inhibit the predominant reading response, and instead name the color of the ink. In the fourth condition, Inhibition/Switching, some words are written inside a frame, and some are not. For words without frames, the participant is to do as in the third condition, name the color of the ink. When the word is framed, s/he has to switch to reading the written word. Thus, this last condition provides a measure of mental flexibility. Scores for all four conditions reflect the number of seconds to complete the task, where lower scores indicate higher speed of completion and thus better performance. To assess inhibition independent from color naming speed, we calculated Condition 3 minus Condition 1 completion time. Similarly, to assess flexibility independent *of* inhibition, we calculated Condition 4 minus Condition 3 completion time.

Conners' continuous performance test II (CPT-II)

The Conners' Continuous Performance Test (2nd ed.; CPT-II; Conners, 2002) is designed to assess visual sustained attention. During the test, the participant is placed in front of a computer with letters flashing on the screen for either 1, 2, or 4 seconds. S/he is asked to press a key every time a letter appears on the screen, except for the letter "X", where pressing the key should be avoided. The number of commission errors (i.e. pressing the key when seeing "X") provides a quality estimate of inhibition ability, with a higher number of errors meaning lower inhibition abilities, as the response to press the key must be inhibited each time X is presented. Standardized scores were used since these were considered to provide more clinical information compared to the raw scores measured in milliseconds on this test.

California verbal learning test (CVLT)

The CVLT is designed to measure verbal memory (Delis, Kramer, Kaplan, & Ober, 1987). The sum of correctly recalled words on the five trials was used to estimate verbal learning abilities, while the number of correctly recalled words after the 20 minutes delay was used as a measure of verbal long-term memory.

D-KEFS towers test

The D-KEFS Towers test was used to measure planning ability (Delis et al., 2001). For each trial, participants are given a base with disks placed in a prearranged manner and are shown a picture of a tower model to reproduce. They are given specific rules, including instruction to build the tower using as few moves as possible. With each trial, the problems become more difficult. Participants are given 30–240 seconds to complete each tower, depending on the model's difficulty level. The total performance score was extracted, with higher scores indicating better planning ability. In addition to planning ability, this tests requires maintaining the planned strategy in working memory for successful problem resolution.

Self-report measures

The self-report assessment covered self-perceptions of executive functioning and ruminative thoughts.

Behavior rating inventory of executive function-adult (BRIEF-A)

The BRIEF-A is a 75-item questionnaire designed to assess subjectively experienced difficulties with executive functioning in everyday life (Roth, Isquith, & Gioia, 2005; Norwegian translation; Nicholas & Solbakk, 2006). Each item covers a difficulty, and participants are asked to rate the frequency of the difficulty as "never", "sometimes" or "often." BRIEF-A provides nine executive functioning component scores, which have been validated in adults (Roth et al., 2005). We used the BRIEF-A Working Memory (e.g. "I have trouble with doing more than one thing at a time") and the BRIEF-A Inhibition (e.g. "People say I'm easily distracted") components, both of which consist of eight items. For each score, responses are summed, with higher scores representing lower functioning. The participant's score is compared to healthy normative data to yield a *t*-score, to permit results' interpretation, with values of 65 or higher indicating an executive functioning problem.

Rumination response scale (RRS)

The 22-item RRS is designed to assess the current degree of ruminative responses to dysphoric mood (Treynor, Gonzalez, & Nolen-Hoeksema, 2003). We used a Norwegian translation of this scale. Each item is rated on a scale from 1 (almost never) to 4 (almost always) to yield a sum score between 22 and 88, where higher scores reflect higher levels of rumination (Roelofs, Muris, Huibers, Peeters, & Arnts, 2006). The RRS consists of three subscales: Depression-related thoughts (12 items), Brooding (5 items), and Reflection (5 items). The Depression-related thoughts subscale has shown significant association with core symptoms of depression (e.g. "think about how passive and unmotivated you feel"; "think about all your shortcomings, failings, faults, mistakes"). The Brooding subscale intends to capture "moody pondering" (Treynor et al., 2003), which includes both self-criticizing thoughts and more general gloomy thoughts (e.g. "think 'What am I doing to deserve this?'"). The Reflection subscale covers use of purposeful reflection to resolve depression-associated issues (e.g. "analyze your personality to try to understand why you are depressed"). The latter two subscales have been found to relate to current and future depression (Treynor et al., 2003).

Rumination-reflection questionnaire (RRQ)

The RRQ is a 24-item self-report scale designed to assesses the degree to which an individual tends to engage in self-attentive reflection in general (as opposed to specifically in relation to depressive mood, which is captured by the RRS) (Trapnell & Campbell, 1999). A Norwegian translation was administered. The RRQ consists of two subscales: Rumination covering repetitively dwelling on perceived faults, injustices or past experiences (e.g. "I often reflect on episodes in my life that I should no longer concern myself with") and Reflection covering curiosity toward exploring the inner self (e.g. "I love exploring my 'inner' self"). Each item of the RRQ is rated on a scale from 1 ("strongly disagree") to 5 ("strongly agree"). Both subscales have shown high coefficient alphas (Trapnell & Campbell, 1999). The Rumination subscale was shown to correlate highly with neuroticism whereas the Reflection subscale was associated with openness to experience (Trapnell & Campbell, 1999).

Statistical methods

Analyses were performed using SPSS version 25 (IBM, Montauk, NY).

To examine baseline predictors of attrition, independent sample *t*-tests were conducted to compare those who did and those who did not complete the study. Remaining analyses were based on completers only. Descriptive statistics were used to estimate the Cogmed-derived scores of percent training improvement, subjective motivation, and percent of personal goals achieved during training. Between-group comparisons on gender and hand dominance ratios were examined with chi-square tests. Paired sample *t*-tests were conducted to examine change in objective (neuropsychological tests) and self-report variables. Effect sizes of pre-post change in performance were coded as positive to indicated improvement relative to pretreatment level and negative to indicate lower performance relative to pretreatment levels. Pearson's product moment correlation coefficients were calculated to identify the relationships among these variables. Two-tailed analyses were conducted, with *p*-value of significance set at 0.05.

Results

Findings concerning feasibility

Thirty-seven individuals contacted the study team with an interest in participating in the study. Among them, five did not attend screening as their availability to enter the study changed, and four had not achieved a sufficient duration of remission (at least two months). The remaining 28 participants entered the study (19 women and 9 men), with a mean age of 35.9 years ($SD = 11.2$, range 20–61) and a mean of 16.1 years of education ($SD = 1.8$; range 13–19). All participants had previously been diagnosed with MDD and been in recovery for at least 2 months: mean MADRS = 4.9 ($SD = 3.0$; range 0–11). None of the patients had ever received electroconvulsive therapy. From the 28 recruited participants, 19 completed the intervention and 18 returned for post-treatment (T2) assessment. That is, nine participants attrited during study training and a tenth completed all 25 sessions but did not return for the T2 (post-intervention) assessment. Table 1 presents the baseline characteristics of the whole sample and statistical comparisons between completers and non-completers on these characteristics. There was no significant between-group difference on any demographic, neuropsychological, self-report or clinical variable with the exception of the RRQ, where completers showed significantly higher scores at baseline than non-completers ($p = 0.001$).

Do people with remitted MDD find working memory targeted CR (WM-CR) acceptable?

The overall Cogmed percent training mean improvement score was 51.8% (SD = 16.5; range 19.2%–77.6%). Categorization by the software indicated that 15 of completers (83%) showed high motivation, 2 (11%) showed average motivation and 1 (6%) showed low motivation. At the end of the program, 5 participants (28%) achieved all three personal goals related to the trained cognitive function, 3 (16%) achieved two of these goals, 9 (50%) achieved one goal and 1 (6%) achieved none of the three goals. The most frequently chosen (by 44% of completers) goal was "Staying focused for longer periods of time", which was achieved by 75% of participants who chose it (6/8). All participants who chose the following goals achieved them: "Learning and understanding better when I read", "Not being distracted from a task", and "Not day dreaming during work or other activities that require my attention". Details on goal chosen and their completion are shown in Table 2.

Do objective and self-report working memory and inhibition performance improve following WM-CR and are objective cognitive improvements specific to the targeted functions or generalizable to others?

Post-intervention performance on all variables and significance of change in performance are presented in Table 3.

Post-intervention performance was significantly improved relative to baseline on the following objective outcomes: Digit Span Backward ($d = 0.573$), CWIT Color Naming

Table 1. Full recruited sample baseline characteristics and between-group comparisons of completers versus non completers.

Variable	Completers, $n = 18$, mean (SD)[a]	Non-completers, $n = 10$, mean (SD)[a]	Between-group differences
Age (years)	36.7 (12.8)	34.6 (8.0)	$t = 0.46$, $p = 0.65$
Gender (female vs. male)	11 vs. 7	8 vs. 2	$\chi^2 = 1.052$, $p = 0.31$
Education (years)	16.4 (1.8)	15.7 (1.8)	$t = 0.98$, $p = 0.34$
Hand dominance (right vs. left)	15 vs. 3	10 vs. 0	$\chi^2 = 1.867$, $p = 0.17$
WASI IQ	114.5 (8.3)	117.3 (7.6)	$t = 0.88$, $p = 0.39$
Depressive symptoms (MADRS)	4.6 (3.1)	6.0 (2.9)#	$t = 0.94$, $p = 0.36$
Digit span total	16.8 (3.5)	17.5 (3.1)	$t = 0.50$, $p = 0.62$
Digit span forward	9.8 (2.0)	10.1 (2.6)	$t = 0.31$, $p = 0.76$
Digit span backward	7.0 (1.9)	7.4 (1.6)	$t = 0.56$, $p = 0.58$
CWIT color naming	29.9 (5.1)	27.4 (2.8)	$t = 1.42$, $p = 0.17$
CWIT inhibition	50.2 (11.0)	51.9 (9.8)	$t = 0.40$, $p = 0.69$
CWIT Flexibility	53.3 (8.7)	51.1 (13.3)	$t = 0.53$, $p = 0.60$
CPT commissions	53.3 (12.3)º	54.1 (13.5)	$t = 0.17$, $p = 0.87$
BRIEF-A working memory	15.2 (4.8)	16.0 (4.0)##	$t = 0.42$, $p = 0.68$
BRIEF-A inhibition	11.7 (2.6)	12.4 (2.7)##	$t = 0.72$, $p = 0.48$
Rumination response scale	48.3 (14.2)	47.4 (13.5)	$t = 0.16$, $p = 0.88$
Ruminative-reflection questionnaire	85.9 (12.4)	69.2 (7.8)##	$t = 3.67$, $p = 0.001$

[a]Except for gender and handedness where frequencies are reported.
#$n = 5$; ##$n = 9$; º$n = 17$.
BRIEF-A: behavior rating inventory of executive functions-adult; CPT = Conner's continuous performance test II (T-scores); CWIT = color word interference test; MADRS: Montgomery Åsberg depression rating scale; WASI IQ: Wechsler's abbreviated scales of intelligence intellectual quotient.

Table 2. Working memory training-associated personal goals' achievement.

Goal	Participants who chose this goal	Participants who attained this goal	Percent participants who attained this goal (%)
Staying focused for longer periods of time	8	6	75
Initiating tasks that require focus, e.g. paying bills without procrastination	7	3	43
Staying focused on what people are saying	6	3	50
Keeping my chain of thought until the end of the task	6	1	17
Learning and understanding better when I listen	4	3	75
Keeping track of my things	4	1	25
Learning and understanding better when I read	3	3	100
Not being distracted from a task	3	3	100
Not day dreaming during work or other activities that require my attention	3	3	100
Taking responsibility over my planning and time schedule	3	2	67
Remembering multi-step instructions that are given to me	3	1	33
Solving problems on my own	3	1	33
Organizing my things	1	0	0

Table 3. Post-intervention cognitive and self-report performance, paired *t*-test comparisons with corrsponding baseline and mean changes in performance.

Variable	Post-intervention mean (SD)	Paired *t*-tests with significance values	Change in performance[a]	
			Mean (SD)	95% Confidence interval
Digit span forward	10.72 (2.2)	$t = 1.95$, $p = 0.068$	0.89 (1.9)	−0.07 to 1.85
Digit span backward	8.39 (2.9)	$t = 2.43$, $p = 0.027$	1.39 (2.4)	0.18 to 2.60
CWIT color naming	27.78 (5.5)	$t = 2.96$, $p = 0.009$	2.11 (3.0)	0.61 to 3.62
CWIT inhibition	44.61 (8.4)	$t = 4.49$, $p < 0.001$	5.61 (5.3)	2.97 to 8.25
CWIT flexibility	49.50 (9.1)	$t = 1.99$, $p = 0.063$	3.78 (8.1)	−0.24 to 7.79
CWIT inhibition—color naming	16.83 (5.5)	$t = 2.79$, $p = 0.013$	3.50 (5.3)	0.85 to 6.15
CWIT flexibility—inhibition	4.89 (6.6)	$t = 0.77$, $p = 0.45$	−1.83 (10.1)	−6.86 to 3.20
CPT commissions	49.40 (11.0)	$t = 2.76$, $p = 0.014$	3.86 (5.8)	0.90 to 6.82
CVLT learning (total trial 1 to 5)	65.89 (10.1)	$t = 4.18$, $p = 0.001$	11.83 (12.0)	5.87 to 17.80
CVLTdelayed recall	14.50 (2.3)	$t = 2.64$, $p = 0.017$	1.00 (1.6)	0.20 to 1.80
Towers test	20.33 (4.4)	$t = 1.75$, $p = 0.10$	1.67 (4.0)	−3.68 to 0.34
BRIEF-A working memory	14.83 (3.3)	$t = 0.56$, $p = 0.58$	0.39 (3.0)	−1.08 to 1.86
BRIEF-A inhibition	11.44 (2.5)	$t = 0.44$, $p = 0.67$	0.22 (2.2)	−0.85 to 1.30
RRS full scale	46.17 (15.1)	$t = 0.50$, $p = 0.62$	2.11 (17.8)	−6.74 to 10.96
RRS depression-related thoughts	26.06 (9.5)	$t = 0.17$, $p = 0.87$	0.39 (9.9)	−4.51 to 5.29
RRS brooding	10.39 (3.8)	$t = 1.03$, $p = 0.31$	1.00 (4.1)	−1.04 to 3.04
RRS reflection	9.72 (3.5)	$t = 0.64$, $p = 0.53$	0.72 (4.8)	−1.66 to 3.11
RRQ full scale	81.94 (11.8)	$t = 1.39$, $p = 0.18$	4.00 (12.2)	−2.06 to 10.06
RRQ rumination	40.00 (9.8)	$t = 1.35$, $p = 0.20$	2.89 (9.1)	−1.64 to 7.42
RRQ reflection	41.94 (7.9)	$t = 0.96$, $p = 0.35$	1.11 (4.9)	−1.34 to 3.56

[a]Coded positive to indicated improvement relative to pretreatment level and negative to indicate lower performance relative to pretreatment levels.
BRIEF-A: behavior rating inventory of executive functions-adult; CPT: Conner's continuous performance test II (T-scores); CVLT: California verbal learning test; CWIT: Color word interference test; RRS: rumination response scale; RRQ: ruminative-reflection questionnaire.

Table 4. *Post hoc* comparsisons between participants whose Digit Span Backwards performance improved by gaining at least 2 points (WM improvers, $n = 10$) and those who did not (WM non-improvers, $n = 8$).

Change on score in varaible	WM improvers, mean (SD)[a]	WM non-improvers, mean (SD)[a]	Between-group differences
RRS full scale	5.3 (14.1)	−11.4 (18.4)	$t = 2.18$, $p = 0.044$
RRS depression-related thoughts	4.0 (7.6)	−5.8 (10.0)	$t = 2.39$, $p = 0.031$
RRS brooding	−0.1 (3.9)	−2.1 (4.4)	$t = 1.04$, $p = 0.31$
RRS reflection	1.4 (3.7)	−3.4 (4.9)	$t = 2.36$, $p = 0.030$
RRQ full scale	−0.6 (10.2)	−8.3 (13.8)	$t = 1.36$, $p = 0.19$
RRQ rumination	−0.4 (8.6)	−6.0 (9.4)	$t = 1.32$, $p = 0.20$
RRQ reflection	−0.2 (4.1)	−2.3 (5.9)	$t = 0.87$, $p = 0.40$
Sociodemographic and clinical characteristics of the subgroups			
Age (years)	37.6 (14.3)	35.5 (11.5)	$t = 0.34$, $p = 0.74$
Education (years)	16.4 (1.5)	16.4 (2.1)	$t = 0.029$, $p = 0.98$
Gender (ratio female vs. male)	6 vs. 4	5 vs. 3	$\chi^2 = 0.012$, $p = 0.91$
IQ	116.6 (9.3)	111.9 (6.4)	$t = 1.22$, $p = 0.24$
Pretreatment MADRS	5.4 (2.7)	3.5 (3.3)	$t = 1.33$, $p = 0.20$

[a]Coded positive to indicated improvement relative to pretreatment level and negative to indicate lower self-report relative tro pretreatment levels.
RRS: rumination response scale; RRQ: ruminative-reflection questionnaire.

($d = 0.367$), CWIT Inhibition ($d = 1.059$), CWIT Inhibition – Color Naming ($d = 0.657$), CPT commissions ($d = 0.671$), CVLT learning ($d = 0.985$) and CVLT delayed recall ($d = 0.623$). Although mean differences were higher post-intervention (i.e., less reported executive function lapses and less rumination), none of these improvements reached significance (all $ps > 0.18$).

Objective improvement was observed on measures of targetted cognitive functions: Digit Span Backward for working memory, CPT commissions for quality of inhibition and CWIT Inhibition for speed of inhibition. There was also a significant improvement on speed on the simple color naming task. However, the variable measuring speed of inhibition independent from speed of color naming (CWIT Inhibition – Color Naming) also showed significant improvement. Overall, there was no significant improvement on other measures of untrained cognitive functions, with the exception of the verbal memory variables (CVLT learning and CVLTdelayed recall).

Are post-WM-CR cognitive improvements associated with decreased rumination?

There was no significant decrease on any rumination measure relative to baseline (all $ps > 0.18$). Also, there were no significant associations between change in rumination and change in any objective cognitive variable where significant improvements were observed (all $ps > 0.10$).

To further explore the effects of improved WM on changes in rumination, we conducted *post hoc* comparisons between WM improvers (T2 score on the Digit Span Backwards improved by 2 points or more from T1) and WM non-improvers (Digit Span Backwards change <2 points of improvement). WM improvers had significantly larger improvements on all RRS variables except RRS brooding than WM non improvers. However, both groups showed comparable change of performance on all RRQ variables (all p-values >0.19). See full *post-hoc* results in Table 4.

If any, which baseline characteristics can explain the targeted cognitive improvement?

Correlation analyses of sociodemographic (age, gender, years of education) and IQ variables showed that positive change in CWIT Inhibition independent from speed correlated with age ($r = 0.47$, $N = 18$, $p = 0.024$, $d = 1.065$) and years of education ($r = 0.66$, $N=18$, $p = 0.001$, $d = 1.776$). Change in other targeted cognitive variables was not significantly related to sociodemographic or IQ data (all $ps > 0.11$).

Discussion

To our knowledge, this is the first study to explore pilot data and investigate the feasibility of cognitive remediation targeting working memory (WM) in formerly depressed individuals. We examined the feasibility of a highly intensive program consisting of 25 sessions and weekly coaching. The majority participants' (68%) who enrolled in the study completed all sessions, and all but one of these completed the end-of-treatment assessment (T2). The completion rates are consistent with those observed in other studies of CR in depression (Motter et al., 2016) and also with the pilot of Semkovska and Ahern (2017) in remitted depression. In addition to completion and adherence rates, we also collected data on the participants motivation, which has not previously been assessed in studies of CR in depression. Motivation during the intervention was high. Specifically, 83% of completers reported high motivation. On average, participants increased their initial WM performance on Cogmed by 50%, with the lowest increase being of 19.2%. At baseline, individuals who completed the intervention showed significantly higher general rumination/reflection (RRQ) than non-completers, while being comparable on all other objective and subjective measures, including current ruminative responses to dysphoric mood (RRS). This indicates that those who continue to struggle with rumination after remission may be more motivated to pursue the intervention. It could also be due to trait characteristics like personality factors influencing willingness to comply with the intervention (Jaeggi, Buschkuehl, Shah, & Jonides, 2014).

Objective cognitive measures showed that participants improved on all measures of targeted functions: Digit Span Backwards for WM, CPT commissions for accuracy of inhibition and the CWIT variables for speed of inhibition. However, this was not reflected in the subjective assessments of Working Memory and Inhibition, as assessed using the BRIEF-A scales. These results are consistent with abundant literature in depression showing a lack of association between objective and subjective measure of cognition (e.g. Beblo, Kater, Baetge, Driessen, & Piefke, 2017; Moritz, Ferahli, & Naber, 2004; Petersen, Porter, & Miskowiak, 2019). Nevertheless, participants did experience some improvement as demonstrated by their levels of personal goals achieved: only one participant did not reach at least one WM and inhibition-related goal. Furthermore, cognitive improvement in WM and inhibition generalized to verbal episodic memory, both immediate and delayed recall, but not to other aspects of executive function (shifting as measured by CWIT flexibility or planning as measured by D-KEFS Towers). These findings suggest that the improvement in WM might have led to better encoding and consolidation of the information, promoting improved delayed verbal memory recall. Although shifting and planning also depend on WM, performance on these two domains did not improve significantly. This may be because these domains are also heavily dependent on executive functions which were not targeted by the present intervention. The observed targeted cognitive improvement along with its selective generalization to long-term memory supports the validity of the intervention.

Overall, WM improvements did not correlate with any measure of change in rumination. Compared to WM non-improvers, however, participants who significantly increased their objective WM performance relative to baseline showed less *current* ruminative responses to dysphoric mood as shown by improved RRS total score, RRS Depression-related thoughts subscale score and RRS Reflection subscale score. WM improvers and WM non-improvers were comparable on all RRQ variables and on RRS Brooding. Thus, a significant improvement in WM at the individual level is related to less rumination linked to depressive mood, without having an effect on general self-attentive reflection. Indeed, the RRQ conceptualises self-reflection as an adaptative, thus positive, mechanism of self-focused thoughts (Trapnell & Campbell, 1999), whereas the RRS is designed to capture pathogenic rumination. The sample size does, however, make it difficult to draw any clear conclusions. Further explorations of these results should be made in a full-trial and could have consequences for screening of participants and ethical considerations that need to be made. Sociodemographic and IQ factors did not explain any targeted cognitive improvement, except for inhibition independent of speed where both older and more educated participants showed larger improvements.

Limitations

The main limitations of the study are inherent to the pilot design – conclusions are tentative until confirmed by a full-scale trial. Generalizability to less self-reflective depressive remitters than the final completers sample also needs verification by future research. It is also important to note that some researchers have questioned to what extent effects of WM CR programs generalize to everyday life (Melby-Lervåg & Hulme, 2013; Shipstead, Hicks, & Engle, 2012), and we did not gather indices of daily function. Moreover, one has to consider possible learning effects in a pre-post study and given the relatively short time between assessments at T1 and T2, approximately a mean period of 10 weeks, practice effects on the tests cannot be ruled out (Calamia, Markon, & Tranel, 2012), however, the apparent selectivity of the effects to WM measures suggests that this cannot fully explain the changes in the present study.

Moreover, the study could have been strengthened by including data on the dose-response relationships, however, there was insufficient range in dose to evaluate. This should be considered in future studies.

In addition, concerning the rumination data, one have to take into consideration that the sample is small and the results could be interpreted as counterintuitive and to be due to a type I error. The data should be conducted analyzed in a larger sample. Finally, the current pilot study did not compare the effects of CR to a control group making it difficult to differentiate between general and specific effects. However, this limitation will be resolved by the planned full-scale trial. A full-scale trial should also aim to determine if the significant improvements are clinically meaningful by using the validated Reliable Change Index (Jacobson & Truax, 1991), which could also address the issue around some significant results being partly explained by practice effects. Another interesting and important question to explore further in a full-scale trial is the association between time in remission and degree of improvement in order to detect an optimal spot of improvement after last episode.

In conclusion, the present pilot study indicates that WM-targeted CR over five weeks for individuals remitted from depression is feasible, with satisfactory levels of participant-experienced acceptability. The intervention selectively improved targeted and directly dependent cognitive functions and, for individuals whose WM was significantly enhanced, it also decreased dysphoric-mood related rumination, a known predictor of relapse. These results provide a foundation for considering whether WM targeted CR intervention, as compared to a control condition, could be an acceptable and a cost-effective tool to prevent relapse and recurrence in major depression.

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References

Ahern, E., & Semkovska, M. (2017). Cognitive functioning in the first-episode of major depressive disorder: A systematic review and meta-analysis. *Neuropsychology*, *31*(1), 52–72. doi:10.1037/neu0000319

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: American Psychiatric Association.

Baune, B. T., Miller, R., McAfoose, J., Johnson, M., Quirk, F., & Mitchell, D. (2010). The role of cognitive impairment in general functioning in major depression. *Psychiatry Research*, *176*(2–3), 183–189. doi:10.1016/j.psychres.2008.12.001

Beblo, T., Kater, L., Baetge, S., Driessen, M., & Piefke, M. (2017). Memory performance of patients with major depression in an everyday life situation. *Psychiatry Research*, *248*, 28–34. doi:10.1016/j.psychres.2016.12.013

Bellander, M., Brehmer, Y., Westerberg, H., Karlsson, S., Furth, D., Bergman, O., Eriksson, E., & … Äckman, L. (2011). Preliminary evidence that allelic variation in the LMX1A gene influences training-related working memory improvement. *Neuropsychologia*, *49*(7), 1938–1942. doi:10.1016/j.neuropsychologia.2011.03.021

Biesheuvel-Leliefeld, K. E., Kok, G. D., Bockting, C. L., Cuijpers, P., Hollon, S. D., van Marwijk, H. W., & Smit, F. (2015). Effectiveness of psychological interventions in preventing recurrence of depressive disorder: Meta-analysis and meta-regression. *Journal of Affective Disorders*, *174*, 400–410. doi:10.1016/j.jad.2014.12.016

Bosnes, O. (2009). Norsk versjon av Wechsler Abbreviated Scale of Intelligence: Hvor godt er samsvaret mellom WASI og norsk versjon av Wechsler Adult Intelligence Scale-III. *Tidsskrift for Norsk Psykologforening*, *46*(6), 4.

Buist-Bouwman, M. A., Ormel, J., de Graaf, R., de Jonge, P., van Sonderen, E., Alonso, J., Bruffaerts, R., & Vollebergh, W. A. M., The ESEMeD/MHEDEA 2000 investigators. (2008). Mediators of the association between depression and role functioning. *Acta Psychiatrica Scandinavica*, *118*(6), 451–458. doi:10.1111/j.1600-0447.2008.01285.x

Calamia, M., Markon, K., & Tranel, D. (2012). Scoring higher the second time around: Meta-analyses of practice effects in neuropsychological assessment. *The Clinical Neuropsychologist*, *26*(4), 543–570.

Christopher, G., & MacDonald, J. (2005). The impact of clinical depression on working memory. *Cognitive Neuropsychiatry*, *10*(5), 379–399. doi:10.1080/13546800444000128

Cogmed. (2016). *Cogmed research*. Retrieved from http://www.cogmed.com/research.

Conners, C. K. (2002). *Conners' continuous performance test (CPTII). Technical guide and software manual*. North Tonawanda, NY: Multi Health Systems.

Delis, D., Kaplan, E., & Kramer, J. H. (2001). *Examiner's maunal of the Delis-Kaplan Executive Functioning System*. San Antonio, TX: The Psychological Corporation.

Delis, D., Kramer, J. H., Kaplan, E., & Ober, B. A. (1987). *CVLT, California verbal learning test: Adult version: Manual*. San Antonio, TX: The Psychological Corporation.

Figueroa, C., Ruhé, H., Koeter, M., Spinhoven, P., Van Der Does, W., Bockting, C., & Schene, A. (2015). Cognitive reactivity versus dysfunctional cognitions and the prediction of relapse in recurrent major depressive disorder. *The Journal of Clinical Psychiatry*, *76*(10), E1306–12. doi:10.4088/JCP.14m09268

Gohier, B., Ferracci, L., Surguladze, S. A., Lawrence, E., El Hage, W., Kefi, M. Z., Allain, P., … LeGall, D. (2009). Cognitive inhibition and working memory in unipolar depression. *Journal of Affective Disorders*, *116*(1–2), 100–105. doi:10.1016/j.jad.2008.10.028

Gonda, X., Pompili, M., Serafini, G., Carvalho, A., Rihmer, Z., & Dome, P. (2015). The role of cognitive dysfunction in the symptoms and remission from depression. *Annals of General Psychiatry*, *14*(1), 27. doi:10.1186/s12991-015-0068-9

Gotlib, I. H., & Joormann, J. (2010). Cognition and depression: Current status and future directions. *Annual Review of Clinical Psychology*, *6*(1), 285–312. doi:10.1146/annurev.clinpsy.121208.131305

Hammar, Å., & Årdal, G. (2009). Cognitive functioning in major depression-a summary. *Frontiers in Human Neuroscience*, *3*, 1–7. doi:10.103389/neuro.09.026.2009

Hays, J. R., Reas, D. L., & Shaw, J. B. (2002). Concurrent validity of the Wechsler abbreviated scale of intelligence and the Kaufman brief intelligence test among psychiatric inpatients. *Psychological Reports*, *90*(2), 355–359. doi:10.2466/pr0.2002.90.2.355

Jacobson, N. S., & Truax, P. (1991). Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology*, *59*(1), 12–19. doi:10.1037/0022-006X.59.1.12

Jaeger, J., Berns, S., Uzelac, S., & Davis-Conway, S. (2006). Neurocognitive deficits and disability in major depressive disorder. *Psychiatry Research*, *145*(1), 39–48. doi:10.1016/j.psychres.2005.11.011

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Shah, P. (2012). Cogmed and working memory training—Current challenges and the search for underlying mechanisms. *Journal of Applied Research in Memory and Cognition*, *1*(3), 211–213. doi:10.1016/j.jarmac.2012.07.002

Jaeggi, S. M., Buschkuehl, M., Shah, P., & Jonides, J. (2014). The role of individual differences in cognitive training and transfer. *Memory and Cognition*, *42*(3), 464–480. doi:10.3758/s13421-013-0364-z

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. doi:10.1007/s10608-006-9035-8

Joormann, J., & Gotlib, I. H. (2010). Emotion regulation in depression: Relation to cognitive inhibition. *Cognition and Emotion*, *24*(2), 281–298. doi:10.1080/02699930903407948

Joormann, J., Levens, S. M., & Gotlib, I. H. (2011). Sticky thoughts: Depression and rumination are associated with difficulties manipulating emotional material in working memory. *Psychological Science*, *22*(8), 979–983. doi:10.1177/0956797611415539

Joormann, J., Yoon, K. L., & Zetsche, U. (2007). Cognitive inhibition in depression. *Applied and Preventive Psychology*, *12*(3), 128–139. doi:10.1016/j.appsy.2007.09.002

Kasper, S., & Eder, H. (1994). Who should benefit from long-term antidepressant therapy? In J. Mendlewicz & A. Glassmann (Eds.), *Depression as a lifetime disorder. Proceedings from XIX CIPN Congress*, (pp. 17–28). Washington, DC.

Klingberg, T., Fernell, E., Olesen, P. J., Johnson, M., Gustafsson, P., Dahlstrom, K., … Westerberg, H. (2005). Computerized training of working memory in children with ADHD—A randomized, controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry*, *44*(2), 177–186. doi:10.1097/00004583-200502000-00010

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. doi:10.1076/jcen.24.6.781.8395

Koster, E., Hoorelbeke, K., Onraedt, T., Owens, M., & Derakshan, N. (2017). Cognitive control interventions for depression: A systematic review of findings from training studies. *Clinical Psychology Review*, *53*, 79–92. doi:10.1016/j.cpr.2017.02.002

Kuehner, C., & Huffziger, S. (2012). Response styles to depressed mood affect the long-term course of psychosocial functioning in depressed patients. *Journal of Affective Disorders*, *136*(3), 627–633. doi:10.1016/j.jad.2011.10.019

Kuehner, C., & Weber, I. (1999). Responses to depression in unipolar depressed patients: An investigation of Nolen-Hoeksema's response styles theory. *Psychological Medicine*, *29*(6), 1323–1333. doi:10.1017/S0033291799001282

Lancaster, G. A., Dodd, S., & Williamson, P. R. (2004). Design and analysis of pilot studies. Recommendations for good practice. *Journal of Evaluation in Clinical Practice*, *10*(2), 307–312. doi:10.1111/j.2002.384.doc.x

Leiknes, K. A., Legange, R. S., Malt, E. A., & Malt, U. (1999). Mini internasjonalt neuropsykiatrisk intervju. In D. Sheehan, J. Janavs, J. Baker, K. Harnett-Sheenan, E. Knapp, & M. Sheehan (Eds.), *Mini international neuropsychiatric interview*. Tampa, FL: University of South Florida.

Marazziti, D., Consoli, G., Picchetti, M., Carlini, M., & Faravelli, L. (2010). Cognitive impairment in major depression. *European Journal of Pharmacology*, *626*(1), 83–86. 10.1016/J.EJPHAR.2009.08.046

McGurk, S. R., Twamley, E. W., Sitzer, D. I., McHugo, G. J., & Mueser, K. T. (2007). A meta-analysis of cognitive remediation in schizophrenia. *American Journal of Psychiatry*, *164*(12), 1791–1802. doi:10.1176/appi.ajp.2007.07060906

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

Melby-Lervåg, M., & Hulme, C. (2013). Is working memory training effective? A meta-analytic review. *Developmental Psychology*, *49*(2), 270–291. doi:10.1037/a0028228

Millan, M. J., Agid, Y., Brüne, M., Bullmore, E. T., Carter, C. S., Clayton, N. S., … Young, L. J. (2012). Cognitive dysfunction in psychiatric disorders: Characteristics, causes and the quest for improved therapy. *Nature Reviews Drug Discovery*, *11*(2), 141–168. doi:10.1038/nrd3628

Montgomery, S. A., & Åsberg, M. (1979). A new depression scale designed to be sensitive to change. *The British Journal of Psychiatry*, *134*(4), 382–389. doi:10.1192/bjp.134.4.382

Moritz, S., Ferahli, S., & Naber, D. (2004). Memory and attention performance in psychiatric patients: Lack of correspondence between clinician-rated and patient-rated functioning with neuropsychological test results. *Journal of the International Neuropsychological Society*, *10*(4), 623–663. doi:10.1017/S1355617704104153

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 and Review*, *18*, 46–60. doi: 46-60. doi:10.3758/s13423-010-0034-0

Motter, J. N., Pimontel, M. A., Rindskopf, D., Devanand, D. P., Doraiswamy, P. M., & Sneed, J. R. (2016). Computerized neuropsychological training and functional recovery in major depressive disorder: A meta-analysis. *Journal of Affective Disorders*, *189*, 184–191. doi:10.1016/j.jad.2015.09.022

Mueller, T. I., Leon, A. C., Keller, M. B., Solomon, D. A., Endicott, J., Coryell, W., … Maser, J. D. (1999). Recurrence after recovery from major depressive disorder during 15 years of observational follow-up. *American Journal of Psychiatry*, *156* (7), 1000–1006. doi:10.1176/ajp.156.7.1000

Nicholas, J., & Solbakk, A. K. (2006). *BRIEF-P Norwegian manual supplement*. Lutz, FL: Psychological Assessment Resources.

Nolen-Hoeksema, S., Wisco, B.E., & Lyubomirsky, S. (2008). Rethinking rumination. *Perspectives on Psychological Science*, *3*(5), 400–424. doi:10.1111/j.1745-6924.2008.00088.x

Otte, C., Gold, S. M., Penninx, B. W., Pariante, C. M., Etkin, A., Fava, M., … Schatzberg, A. F. (2016). Major depressive disorder. *Nature Reviews Disease Primers*, *2*(1), 16065. doi:10.1038/nrdp.2016.65

Pearson. (2016). *Cogmed arbeidsminnetrening*. Retrieved from http://www.cogmed.com/cogmed-training-method.

Peckham, A. D., & Johnson, S. L. (2018). Cognitive control training for emotion-related impulsivity. *Behaviour Research and Therapy*, *105*, 17–26. doi:10.1016/j.brat.2018.03.009

Petersen, J.Z., Porter, R. J., & Miskowiak, K.W. (2019). Clinical characteristics associated with the discrepancy between subjective and objective cognitive impairment in depression. *Journal of Affective Disorders*, *246*, 763–774. doi:10.1016/j.jad.2018.12.105

Porter, R. J., Bowie, C. R., Jordan, J., & Malhi, G. S. (2013). Cognitive remediation as a treatment for major depression: A rationale, review of evidence and recommendations for future research. *The Australian and New Zealand journal of psychiatry*, *12*, 1165–1175. doi:10.1177/0004867413502090

Porter, R. J., Hammar, Å., Beevers, C. G., Bowie, C. R., Nodtvedt, Ø. O., Peckham, A. D., … Vinogradov, S. (2017). Cognitive and affective remediation training for mood disorders. *Australian and New Zealand Journal of Psychiatry,* 51*(4), 317-319*. doi:10.1177/0004867416678079

Prado, C. E., Watt, S., & Crowe, S. F., (2018). A meta-analysis of the effects of antidepressants on cognitive functioning in depressed and non-depressed samples. *Neuropsychology Review*, 2(1), 32–72

Roche, J. D., & Johnson, B. D. (2014). Cogmed working memory training product review. *Journal of Attention Disorders*, *18*(4), 379–384. doi:10.1177/1087054714524275

Roelofs, J., Muris, P., Huibers, M., Peeters, F., & Arntz, A. (2006). On the measurement of rumination: A psychometric evaluation of the ruminative response scale and the rumination on sadness scale in undergraduates. *Journal of Behavior Therapy and Experimental Psychiatry*, *37*(4), 299–313. doi:10.1016/j.jbtep.2006.03.002

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. doi:10.1016/j.neures.2004.05.003

Ronold, E. H., Joormann, J. & Hammar, Å. (2018). Facing recovery: Emotional bias in working memory, rumination, relapse, and recurrence of major depression; An experimental paradigm conducted five years after first episode of major depression. *Applied Neuropsychology: Adult*, *0*(0), 1–12. doi:10.1080/23279095.2018.1550406

Roth, R. M., Isquith, P. K., & Gioia, G. A. (2005). *Behavior rating inventory of executive function-adult version (BRIEF-A)*. Lutz, FL: Psychological Assessment Resources.

Ryan, J. J., Carruthers, C. A., Miller, L. J., Souheaver, G. T., Gontkovsky, S. T., & Zehr, M. D. (2003). Exploratory factor analysis of the Wechsler Abbreviated Scale of Intelligence (WASI) in adult standardization and clinical samples. *Applied Neuropsychology*, *10*(4), 252–256. doi:10.1207/s15324826an1004_8

Schmid, M., & Hammar, A. (2013). A follow-up study of first episode major depressive disorder. Impairment in inhibition and semantic fluency-potential predictors for relapse? *Frontiers in Psychology*, *4*, 633. doi:10.3389/fpsyg.2013.00633

Semkovska, M., & Ahern, E. (2017). Online neurocognitive remediation therapy to improve cognition in community-living individuals with a history of depression: A pilot study. *Internet Interventions*, *9*, 7–14. doi:10.1016/j.invent.2017.04.003

Semkovska, M., Quinlivan, L., O'Grady, T., Johnson, R., Collins, A., O'Connor, J., …., Gload, T. (2019). Cognitive function following a major depressive episode: A systematic review and meta-analysis. *Lancet Psychiatry, 6(10), 851-861.*

Shipstead, Z., Hicks, K. L., & Engle, R.W. (2012). Cogmed working memory training: Does the evidence support the claims? *Journal of Applied Research in Memory and Cognition*, *1*(3), 185–193. doi:10.1016/j.jarmac.2012.06

Shipstead, Z., Redick, T. S., & Engle, R. W. (2012). Is working memory training effective? *Psychological Bulletin*, *138*(4), 628–654. doi:10.1037/a0027473

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. doi:10.1007/s10608-006-9118-6

Siegle, G. J., Price, R. B., Jones, N. P., Ghinassi, F., Painter, T., & Thase, M. E. (2014). You gotta work at it: Pupillary indices of task focus are prognostic for response to a neurocognitive intervention for rumination in depression. *Clinical Psychological Science*, *2*(4), 455–471. doi:10.1177/2167702614536160

Solomon, D. A., Keller, M. B., Leon, A. C., Mueller, T. I., Lavori, P. W., Shea, T., … Endicott, J. (2000). Multiple recurrences of major depressive disorder. *American Journal of Psychiatry*, *157*(2), 229–233. doi:10.1176/appi.ajp.157.2.229

Stegenga, B. T., Kamphuis, M. H., King, M., Nazareth, I., & Geerlings, M. I. (2012). The natural course and outcome of major depressive disorder in primary care: The PREDICT-NL study. *Social Psychiatry and Psychiatric Epidemiology*, *47*(1), 87–95. doi:10.1007/s00127-010-0317-9

Timm, C., Ubl, B., Zamoscik, V., Ebner-Priemer, U., Reinhard, I., Huffziger, S., … Kuehner, C. (2017). Cognitive and affective trait and state factors influencing the long-term symptom course in remitted depressed patients. *PLOS One*, *12*(6), e0178759. doi:10.1371/journal.pone.0178759

Trapnell, P. D., & Campbell, J. D. (1999). Private self-consciousness and the five-factor model of personality: Distinguishing rumination from reflection. *Journal of Personality and Social Psychology*, *76*(2), 284–304. doi:10.1037/0022-3514.76.2.284

Treynor, W., Gonzalez, R., & Nolen-Hoeksema, S. (2003). Rumination reconsidered: A psychometric analysis. *Cognitive Therapy and Research*, *27*(3), 247–259. doi:10.1023/A:1023910315561

Vittengl, J. R., Clark, L. A., Dunn, T. W., & Jarrett, R. B. (2007). Reducing relapse and recurrence in unipolar depression: A comparative meta-analysis of cognitive-behavioral therapy's effects. *Journal of Consulting and Clinical Psychology*, *75*(3), 475–488. doi:10.1037/0022-006X.75.3.475

Wechsler, D. (1997). *The Wechsler memory scale*. San Antonio, TX: The Psychological Corporation.

Whitmer, A. J., & Gotlib, I. H. (2012). Switching and backward inhibition in major depressive disorder: The role of rumination. *Journal of Abnormal Psychology*, *121*(3), 570–578. doi:10.1037/a0027474

World Medical Association. (2009). *Declaration of Helsinki. Ethical principles for medical research involving human subjects.* Retrieved from http://www.wma.net/en/30publications/10policies/b3/.

Wykes, T., Huddy, V., Cellard, C., McGurk, S. R., & Czobor, P. (2011). A meta-analysis of cognitive remediation for schizophrenia: Methodology and effect sizes. *American Journal of Psychiatry*, *5*, 472–485. doi:10.1176/appi.ajp.2010.10060855

Zetsche, U., Bürkner, P. C., & Schulze, L. (2018). Shedding light on the association between repetitive negative thinking and deficits in cognitive control – a meta-analysis. *Clinical Psychology Review*, *63*, 56–65. doi:10.1016/j.cpr.2018.06.001