FACULTY OF PSYCHOLOGY
AND EDUCATIONAL SCIENCES

Cognitive control training as preventive intervention in remitted depressed individuals: Research on clinical effectiveness and user experience

Jasmien Vervaeke

Supervisor: Prof. Dr. Ernst H.W. Koster

A dissertation submitted to Ghent University in partial fulfilment of the requirements for the degree of Doctor of Psychology

Academic year 2019–2020

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Chapter 1: General Introduction

This introductory chapter gives a broad overview of major depressive disorder, including its symptoms, prevalence and treatments. Furthermore, current challenges with these treatments will be highlighted with a focus on specific behavior associated with depression, namely cognitive control impairments and rumination. This is followed by a discussion of the importance of impaired cognitive control and possible avenues to ameliorate such impairments. In addition, the advantages and disadvantages of technological avenues for treatment of mental disorders will be discussed. Lastly, we will describe the main aims of this thesis in relation to these constructs and present an outline of the upcoming chapters.

Major Depressive Disorder

Major depressive disorder (MDD) - frequently simply called depression - is characterized by sustained negative affect but its impact regularly extends to the physical, emotional, cognitive, motivational, social, professional, and financial aspects of a person's functioning. In other words, this mental disorder has a huge impact on the whole life of the person suffering from depression, and often also that of his or her immediate environment (e.g., partner, family, friends, colleagues). According to most recent edition of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013), somebody can be diagnosed with MDD if (1) depressed mood, and/or (2) substantial loss of interest or pleasure, are present during most of the day, almost every day, for at least two weeks. Furthermore, three or more of the following symptoms should occur as well in the same period: (3) significant unintentional weight gain or loss, or changed appetite; (4)

insomnia or hypersomnia; (5) psychomotor retardation or agitation; (6) fatigue or lack of energy; (7) inappropriate feelings of worthlessness or guilt; (8) problems with concentrating or decision making; and (9) thoughts of death, suicidal ideation or a suicide plan/attempt. In addition, these symptoms should result in significant distress or impairments in functioning to be able to be diagnosed with MDD. Thus, although depression is characterized with a sustained negative affect, it is accompanied with symptoms in multiple domains.

MDD is not only a severe mood disorder, it is also a common one. Stronger yet, in the United States of America, it is the most common mental disorder (Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012). The risk of a mood disorder in general is at least 30% over the course of a lifetime (Kessler et al., 2012). Currently, more than 350 million people are suffering from depression, which is about 1 in every 25 people, making it the leading cause of disability worldwide and a major contributor to the overall burden of disease on a global scale (World Health Organization, 2018). In Europe, this estimate is 33.3 million people (Gustavsson et al., 2011). Depression occurs more frequently in women than in men and occurs at all ages, but has a median onset at the age of 25 years (Kessler et al., 2012). A meta-analysis combining over a million participants from 30 countries, showed a lifetime prevalence of 10.8%, which was somewhat higher for women compared to men (Lim, Tam, Lu, Ho, Zhang, & Ho, 2018). Similarly, in Spain, a single point prevalence of 8% was found (Arias-de la Torre, Vilagut, Martin, Molina, & Alonso, 2018). A longitudinal study in Finland calculated a slightly lower prevalence, but also showed that over the course of eleven years, this prevalence increased from 7.3% to 9.6% (Markkula et al., 2015), and it is thought that these prevalence rates will keep increasing.

Importantly, next to the individual suffering, depression is also associated with high costs for the patient, the surrounding environment, and society (for a review, see Luppa, Heinrich, Angermeyer, Konig, & Riedel-Heller, 2007). Financially speaking, costs can be

direct (e.g., related to treatment) or indirect (e.g., related to productivity loss at work). In Europe, costs per year of a broad range of brain disorders are highest for mood disorders at €113.4 billion, and are estimated to be €3406 per patient (Gustavsson et al., 2011). In most cases, the purchasing power of the patient will decrease due to treatment costs. Furthermore, people with mental disorders, including MDD, have a substantially lower income (e.g., Kessler et al., 2008). However, costs of depression reach drastically further than being merely a financial burden. Mood disorders are associated with early termination of secondary education (Lee et al., 2009) and job loss (Dooley, Fielding, & Levi, 1996), which can impact one's entire life. MDD has a high rate of comorbidity with other mental disorders (Rohde, Lewinsohn, & Seeley, 1991; Brown, Campbell, Lehman, Grisham, & Mancill, 2001) and is also found to be a predictor of several chronic physical disorders (such as diabetes and cardiovascular issues; Carnethon, Kinder, Fair, Stafford, & Fortmann, 2003; Van der Kooy, Van Hout, Marwijk, Marten, Stehouwer, & Beekman, 2007). In the presence of depression, these physical disorders regularly know a worse course (Peyrot & Rubin, 1997; Gillen, Tennen, McKee, Gernert-Dott, & Affleck, 2001; Mancuso, Rincon, McCulloch, & Charlson, 2001). In short, MDD is a debilitating mood disorder, that is oft-occurring and has an enormous impact on the patient as well as society.

Fortunately, several evidence-based treatments exist for MDD, for instance psychotherapy (e.g., cognitive behavioral therapy (CBT), interpersonal therapy) and antidepressant medication (e.g., citalopram, venlafaxine), and combining them can lead to an increased effectiveness (for a review on several meta-analyses, see Cuijpers, 2017). These interventions are included in several treatment guidelines, show beneficial effects rather quickly and have an enduring impact after treatment (Karyotaki et al., 2016).

Nevertheless, there are several problems with existing treatments. First, there is an enormous treatment gap, with only a minority of patients with depression actually receiving

treatment (Wang, Lane, Olfson, Pincus, Wells, & Kessler, 2005; Thornicroft et al., 2017). The ones who do not receive treatment, can be treatment-seeking or intentionally not seeking treatment (Thornicroft et al., 2017). In the treatment-seeking sample, factors such as long waiting lists, high costs and practical issues (e.g., insurance, transportation) can prevent them from being treated. Second, in the group receiving treatment, dropout rates are high. Although there are several definitions and measures for dropout (Masi, Miller, & Olson, 2003), in general, *dropout* refers to premature discontinuation of treatment. A meta-analysis showed that mean dropout for psychotherapy is 47% (Wierzbicki & Pekarik, 1993) using a broad definition of dropout. For MDD specifically, this number is thought to range between 20 and 37% (Casacalenda, Perry, & Looper, 2002; Hans & Hiller, 2013; Cooper & Conklin, 2015). Notably, these numbers vary depending on the specific criteria applied to identify dropout, but in all cases a substantial amount of patients does not complete all psychotherapy sessions. Furthermore, psychotherapy effectiveness is dependent of treatment duration (Hansen, Lambert, & Forman, 2002). This is problematic, because independent of effectiveness, dropout prevents patients to benefit from potential effects of any treatment. A third problem is that a subgroup of patients does not respond (sufficiently) to treatment. Indeed, 46% of MDD patients did not reach remission after psychotherapy or pharmaceutical treatment (Casacalenda et al., 2002). Moreover, in a sample that did not respond to a selective serotonin-reuptake inhibitor - a common type of antidepressant medication -, another antidepressant was administered but 70% still failed to reach remission (Rush et al., 2006). Fava and Davidson (1996) estimated that between 19 to 34% of MDD patients is treatment-resistant. Furthermore, psychotherapy is less effective in patients with chronic depression (Cuijpers, Andersson, Donker, & van Straten, 2011), and in patients with comorbid disorders, such as personality disorders (Shea, Widiger, & Klein, 1992) and anxiety disorders (Young, Mufson, & Davies, 2006), but comorbidity is often present. Finally, a subset of MDD patients

does recover. Given the broad impact of depression, this can be defined in several ways, such as an absence of depressive symptomatology, a presence of positive mental health aspects, or a return to the previous level of functioning (Zimmerman, McGlinchey, Posternak, Friedman, Attiullah, & Boerescu, 2006).

However, being in remission does not mean former MDD patients are no longer vulnerable for depression. In contrast, this group has an elevated risk to develop novel depressive episodes and on average, this group develops several episodes during their lifetime (Kessler et al., 2012; Carr & McNulty, 2016). In a group of patients observed for 10 years following remission, Solomon and colleagues (2000) found that 64% of subjects encountered at least one new depressive episode. After 15 years, 35% of remitted depressed individuals suffers from recurrence, and this number is drastically worse for patients treated in specialized centers (i.e., 85%) (Hardeveld, Spijker, De Graaf, Nolen, & Beekman; 2010). These numbers are in line with Bockting, Spinhoven, Koeter, Wouters, & Schene (2006) where 59% of remitted patients showed a recurrence within 2 years. Interestingly, risk of a new episode decreases as the duration of remission increases (Solomon et al., 2000).

Several variables can predict a recurrence, such as the number of previous episodes, residual symptoms and daily hassles (Judd et al., 1998; Solomon et al., 2000; Bockting et al., 2006; Hardeveld et al., 2010). The risk of recurrence increases with 16% with each depressive episode (Solomon et al., 2000) and remitted individuals with subclinical symptoms encounter new depressive episodes with a higher likelihood compared to an asymptomatic group (87% vs. 66% over the course of ten years; Judd et al., 1998). In short, remitted depressed individuals are at risk for developing new episodes. Given this lack of stable remission following a depressive episode, currently existing interventions do not target underlying mechanisms adequately, leaving remitted depressed patients vulnerable for developing new episodes, as expressed by high chances of recurrence.

One of the possible underlying vulnerabilities is emotion regulation. An intervention with emotion regulation training showed enhanced effectiveness of CBT (Berking, Wupperman, Reichardt, Pejic, Dippel, & Znoj, 2008). *Emotion regulation* refers to processes that influence the occurrence, magnitude, duration and expression of an emotional response (Gross, 2014). Given that negative affect is a key feature of depression, it is not surprising that experienced emotions and their regulation can play a key role in onset, maintenance and recurrence of MDD. Regulation strategies can be regarded as adaptive or maladaptive, but using certain strategies is dependent on desired outcomes and contexts, and handling these in a flexible manner is thought to be crucial (Aldao, Nolen-Hoeksema, & Schweizer, 2010). Nevertheless, maladaptive emotion regulation strategies are related more strongly to depressive symptomatology and negative affect, while adaptive strategies are associated with positive mental health indicators (John & Gross, 2004; Hu, Zhang, Wang, Mistry, Ran, & Wang, 2014; Schäfer, Naumann, Holmes, Tuschen-Caffier, & Samson, 2017).

While it is outside the scope of this introduction to go into detail into each strategy separately, one emotion regulation strategy does deserve special attention: rumination (but see Joormann & Stanton, 2016 for a more thorough review). *Rumination* can be regarded as a transdiagnostic factor for several psychological disorders (for a review, see Ehring & Watkins, 2008), yet in the context of MDD specifically, it is defined as the style of thinking that focuses attention on depressive symptoms and the implications of those symptoms (Nolen-Hoeksema, 1991). In other words, after a stressor or negative event, ruminators show a pattern of negative, repetitive, self-referent thoughts, and this hinders recovery from negative mood, prolonging negative affect after distress. Two subtypes of rumination have consistently been found: brooding and reflection (Treynor, Gonzalez, & Nolen-Hoeksema, 2003). *Brooding* refers to moody pondering in a maladaptive, passive and self-critical manner. *Reflection* is viewed as a cognitive problem solving strategy aimed at improving

depressive symptoms. MDD patients ruminate more than healthy controls (Olatunji, Naragon-Gainey, & Wolitzky-Taylor, 2013) and rumination is associated with a wide variety of detrimental phenomena, such as longer and more severe depressive episodes, increased negative mood, impaired problem solving and deficient concentration (for a review, see Nolen-Hoeksema. Wisco, & Lyubomirski, 2008). Furthermore, rumination is a risk factor for depressive symptomatology and depressive episodes (Just & Alloy, 1997; Roberts, Gilboa, & Gotlib, 1998; Kuehner & Weber, 1999). Interestingly, higher levels of rumination are found in groups at risk for depression. Children of mothers with a history of MDD show increased rumination, compared to children of never depressed mothers (Woody, Kudinova, McGeary, Knopik, Palmer, & Gibb, 2016). Remitted depressed women also tend to ruminate more than never depressed women (Woody, McGeary, & Gibb, 2014).

Another possible underlying vulnerability refers to cognitive control impairments. Indeed, MDD is characterized by cognitive deficits in working memory, attention, processing speed and executive functioning (e.g., Austin, Mitchell, & Goodwin, 2001; Rock, Roiser, Riedel, & Blackwell, 2014; Lee, Hermens, Porter, Redoblado-Hodge, 2012) and these are one of the most common symptoms (Conradi, Ormel, & de Jonge, 2011). Furthermore, these deficits often persist during remission from depression and the severity of deficits is correlated with the number of depressive episodes (Paelecke-Habermann, Pohl, & Leplow, 2005; Baune, Miller, McAfoose, Johnson, Quirk, & Mitchell, 2010; Conradi et al., 2011; Rock et al., 2014; Semkovska et al., 2019). Current interventions (such as antidepressant medication) do not improve cognitive functioning sufficiently (Shilyansky, Williams, Gyurak, Harris, Usherwood, & Etkin, 2016; Mackin et al., 2014) and there is some evidence that cognitive impairments during remission can predict recurrence of MDD (Alexopoulos et al., 2000; Majer et al., 2004). These cognitive impairments will be referred to as cognitive control deficits in the remainder of this introduction. *Cognitive control* refers to processes that

regulate and align behaviors and information processing with current goals in an adaptive manner (Botvinick & Braver, 2015). It is thought to be a collection of executive functions that can influence contents in working memory, namely updating/monitoring, shifting, and inhibiting (Miyake, Friedman, Emerson, Witzki, Howeter, & Wager, 2000). Deficits in cognitive control are found in several disorders, including MDD (e.g., Snyder, 2013; Levens & Gotlib, 2010), where especially shifting and inhibition are impaired, rather than the updating/monitoring process. Cognitive control impairments can also be observed in at-risk groups, such as remitted depressed (Levens & Gotlib, 2015; Paelecke-Habermann et al., 2005) and dysphoric individuals (Joormann, 2004; Owens & Derakshan, 2013). These deficits can predict depressive symptomatology and increase vulnerability for developing new episodes (Zetsche & Joormann, 2011; Pe, Brose, Gotlib, & Kuppens, 2016; Kertz, Belden, Tillman, & Luby, 2016) and rumination (Zetsche & Joormann, 2011).

While there has been evidence regarding the existence of a general cognitive control impairment during and after MDD (Snyder, 2013; Semkovska et al., 2019), some argue for cognitive control impairments when processing emotional information specifically (Joormann, Levens, & Gotlib, 2011; Joormann & Gotlib, 2008), showing the intertwined interplay between cognitive control and emotion regulation. Remarkably, effective emotion regulation is thought to depend on cognitive control. Put differently, impairments in cognitive control might lead to difficulties in regulating emotions, for instance rumination (Joormann & D'Avanzato, 2010; Zetsche & Joormann, 2011), and this might mediate the relationship with depressive symptomatology. Specifically, diminished cognitive control causes difficulties removing negative information from working memory, resulting in ruminative thinking. Subsequently, rumination can deplete working memory resources (Whitmer & Gotlib, 2012). Several studies have indeed shown a negative association between cognitive control and rumination in the context of depression, especially with mood-congruent emotional stimuli

(Davis & Nolen-Hoeksema. 2000; Whitmer & Banich, 2007; Donaldson, Lam, & Mathews, 2007; Joormann & Gotlib, 2010; Hilt, Leitzke, & Pollak, 2014; Beckwé, Deroost, Koster, De Lissnyder, & De Raedt, 2014). Particularly, as seen in a plethora of studies investigating memory, interpretation and attention bias, MDD is associated with impaired inhibition of negative information (Joormann, 2004; 2006; for a review, see Joormann, Yoon, & Zetsche, 2007) and impaired disengaging from negative stimuli (Bradley, Mogg, & Lee, 1997; Koster, De Raedt, Goeleven, Franck, & Crombez, 2005; Leyman, De Raedt, Schacht, & Koster, 2006; for a review, see Gotlib & Joormann, 2010). In the case of self-referent negative information, this can lead to prolonged processing of this information, resulting in ruminative thinking and depressive symptomatology, according to the *impaired disengagement hypothesis* (Koster, De Lissnyder, Derakshan, & De Raedt, 2011). This theory treats rumination as a normal response to stressors. In healthy people, ruminating on negative, self-critical thoughts will clash with positive self-views, which causes cognitive conflict. In order to solve this conflict, attention is disengaged from negative thoughts and allows for reappraisal of the situation or a refocus of attention on other, often positive stimuli. However, in depressed patients, conflict signaling or attentional control can be impaired, leading to a disruption of this process, and difficulties with disengaging from negative information are experienced. Moreover, this can lead to impaired problem solving, task impairments and negative affect, and negative thoughts and depressive episodes can be triggered, especially when this thinking style becomes habitual (Koster et al., 2011). Given that both cognitive control impairments and rumination are thought to be vulnerability factors for maintenance and recurrence of MDD, interventions that ameliorate these factors have gained attention. More specifically, as cognitive control impairments are postulated to be underlying rumination, such interventions are exceedingly worth pursuing.

Several studies in the context of MDD have attempted to improve cognitive control and thereby decreasing rumination and depressive symptomatology, by means of *cognitive control training* (CCT). In CCT, tasks that call for cognitive control are administered, often repeatedly and adaptively, over the course of multiple training sessions. By recruiting cognitive control in this manner, impairments are thought to be ameliorated, leading to improved cognitive functioning, adaptive emotion regulation, and decreased depressive symptomatology. To this aim, several tasks have been used in past studies (for an overview, see Koster, Hoorelbeke, Onraedt, Owens, & Derakshan, 2017). The Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977; Siegle, Ghinassi, & Thase, 2007) is one of the most frequently used tasks in this context. Participants hear numbers and need to indicate the sum of every number with the number heard before, while remembering the most recent number in order to correctly perform the next trial. This task relies on cognitive control processes through constantly inhibiting, monitoring and updating information in working memory. A second relevant task here is the dual n-back task (Kirchner, 1958; Jaeggi et al., 2003). Participants are presented with an auditory and a visual stimulus simultaneously, and need to indicate whether a match is present in either or both modalities with stimuli presented *n* trials back. Difficulty can be manipulated by altering the value of *n*. In this task, inhibition, monitoring, and updating of working memory content are necessary as well. Furthermore, flanker tasks have been used in CCT (Cohen et al., 2016). Participants need to respond to the orientation of a target arrow, that is flanked by congruent (same direction) or incongruent (opposite direction) distractor arrows. Incongruent trials call for cognitive control and result in slower reaction times. The magnitude of reaction time slowing in incongruent trials vs. congruent trials (i.e., the congruency effect), can be seen as a measure of cognitive control. Lastly, the negative affective priming task (Tipper, 1985; Joormann, 2004; 2006) consists of paired trials of a prime trial followed by a test trial. Both types of trials contain a target and a

distractor, and participants need to indicate the valence of the target. Cognitive control is necessary on every trial for inhibiting the distractor successfully. Additionally, slowed reaction times are observed when the valence of a distractor of a prime trial is shared with that of the target in a test trial, and this slowing serves as a measure for cognitive control. Provided that the most robust findings have been observed with the PASAT (Koster et al., 2017), we will focus on this task in the remainder of this thesis.

Existing findings are based on a broad variety of implementations of CCT in several samples, leading to inconsistent results (for a review, see Koster et al., 2017). However, meta-analyses showed overall small but beneficial effects in terms of clinical outcomes including self-reported depressive symptomatology (Anaya, Aran, Ayuso-Mateos, Wykes, Vieta, & Scott, 2012; Motter, Pimontel, Rindskopf, Devanand, Doraiswamy, & Sneed, 2016). Indeed, in several studies, CCT has been found to decrease rumination (Siegle, Price, Jones, Ghinassi, Painter, & Thase, 2014; Daches & Mor, 2014; Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015; Vanderhasselt et al., 2015; Hoorelbeke & Koster, 2017) and depressive symptomatology (Siegle et al., 2007; Alvarez, Sotres, León, Estrella, & Sánchez-Sosa, 2008; Brunoni et al., 2014; Iacoviello et al., 2014; Segrave, Arnold, Hoy, & Fitzgerald, 2014; Morimoto, Wexler, Liu, Hu, Seirup, & Alexopoulos, 2014; Calkins, McMorran, Siegle, & Otto, 2015; Hoorelbeke & Koster, 2017), but not consistently (Elgamal, McKinnon, Ramakrishnan, Joffe, & MacQueen, 2007; Onraedt & Koster, 2014; Wanmaker, Geraerts, & Franken, 2015; Trapp, Engel, Haja, Lautenbacher, & Gallhofer, 2016). As this domain is still fairly young, more studies are needed to gain insight into specific mechanisms and develop theories that can explain how CCT can result in beneficial effects on emotion transfer outcomes, despite not showing cognitive transfer (for reviews, see Shipstead, Redick, & Engle, 2012; Melby-Lervåg, Redick, & Hulme, 2016).

Internet-based Interventions for Mental Health

As stated previously, several barriers are present in mental healthcare, resulting in a large dissonance between treatment necessity and treatment delivery. A way to circumvent some of these barriers is by shifting towards internet-based interventions. *Internet-based intervention* is an umbrella term for interventions that aim to prevent, treat, or manage mental disorders, by utilizing the internet for at least one aspect of the intervention. These interventions can be implemented with or without therapist contact and are cost-effective for several mental health disorders, including MDD (Hedman, Andersson, Lindefors, Andersson, Rück, & Ljótsson, 2013; Warmerdam, Smit, van Straten, Riper, & Cuijpers, 2010; Cuijpers, Riper, & Andersson, 2015; Kraepelien et al., 2018). Another advantage is their scalability. Overall, treating MDD patients with individual face-to-face therapy is more time-consuming for therapists, than giving support in internet-based treatments (even though this amount can vary immensely), contributing to longer waiting lists (Cuijpers et al., 2015). By diminishing therapist involvement, more people can receive treatment. The treatment gap has been known to put specific groups at a disadvantage, depending on age, gender, race, disorder, and location (Kohn, Saxena, Levav, & Saraceno, 2004; Rafful, Medina-Mora. Borges, Benjet, & Orozco, 2012; Wagner, Schulz, Knaevelsrud, 2012). Internet-based interventions show potential for reaching people from different backgrounds. Andersson and Titov (2014) observed patients receiving internet-based treatment after several years of showing symptoms without seeking treatment (or even longer in the case of social anxiety disorder). Indeed, the internet is increasingly accessible, with 96% of the population reported having access to the internet in a representative sample in Flanders (Vanhaelewyn & De Marez, 2019). Technological devices are also ubiquitous: in this sample, 80% owned a laptop computer, 39% had a desktop computer and 57% reported having a tablet computer.

Crucially, internet-based interventions are as effective as traditional evidence-based therapies (Ebert et al., 2018). In a randomized controlled trial, there were no differences in treatment outcomes of MDD between CBT delivered face-to-face vs. online (Wagner, Horn, & Maercker, 2014). This is in line with meta-analyses, showing positive effects of internet-based treatments compared to control groups (Andersson & Cuijpers, 2009; Königbauer, Letsch, Doebler, Ebert, & Baumeister, 2017), and equivalent effects compared to face-to-face psychotherapies (Cuijpers, Donker, van Straten, Li., & Andersson, 2010; Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014; Andersson, Topooco, Havik, & Nordgreen, 2016; Carlbring, Andersson, Cuijpers, Riper, & Hedman-Lagerlöf, 2017). Similar to traditional psychotherapy, therapist contact can influence effectiveness (Johansson & Andersson, 2014) but to a lesser extent (Almlöv, Carlbring, Berger, & Andersson, 2009).

While these arguments make internet-based interventions appealing, some disadvantages have been identified. Dropout rates can be upsettingly high in open access internet-based interventions (Christensen, Griffiths, & Farrer, 2009). Frequently, people volunteer to participate in such interventions, but do not begin or drop out early in the treatment (Waller & Gilbody, 2009). For instance, in a community sample with elevated depression scores, only 15.6% of users completed more than one out of five modules of online CBT (Christensen, Griffiths, Korten, Brittliffe, & Groves, 2004), demonstrating a substantial dropout rate early in the intervention. Moreover, Christensen et al. (2004) reported that merely 0.5% completed the full treatment. Adhering to protocol longer shows improved treatment outcomes (Karyotaki et al., 2017) and can be attained through follow-up of users via e-mail (Wangberg, Bergmo, & Johnsen, 2008). Furthermore, dropout in internet-based treatments for MDD can be predicted by elevated baseline depressive symptomatology, older age and more knowledge regarding psychological treatments. Moreover, patients offer several reasons for dropping out, such as low motivation, time constraints, perceived lack of effects,

and improved functioning (review by Christensen et al., 2009). Dropout for the online CBT intervention reported above (Christensen et al., 2004), was predicted by lower symptomatology (depression, anxiety and dysfunctional thinking), older age, lower education, and being male. Furthermore, being referred to the intervention by a mental health professional helped to prevent dropout (Batterham., Neil, Bennett, Griffiths, & Christensen, 2008). These predictors were not fully in agreement with the review of Christensen et al. (2009) and warrant more research.

Early on, dropout has been identified as an issue with internet-based interventions. Eysenbach (2005) proposed several factors that might influence dropout, such as expectation management, usability, workload, and advantages in continued use. However, dropout remained problematic, leading to the founding of the international Collaboration On Maximizing the impact of E-Therapy and Serious Gaming (COMETS). In their perspective article, they call for a paradigm shift to increase the impact of internet-based interventions for mental health, through four aspects of collaboration between researchers, clinicians, developers, and end-users (Fleming et al., 2016). A first aspect calls for user-centered approaches, where end-users have a voice in development and where programs can be individualized. By involving target users in the development, the final product will suit their needs and expectations better. Design and implementation have been implicated in impacting dropout rates (Kelders, Kok, Ossebaard, & van Gemert-Pijnen, 2012; Ludden, van Rompay, Kelders, & van Gemert-Pijnen, 2015) Second, to counter dropout, engagement should be increased by utilizing game elements or increasing immersion. Indeed, engagement and motivation have been identified as a key target for countering dropout in internet-based interventions (e.g., Schubart, Stuckey, Ganeshamoorthy, & Sciamanna, 2011; Doherty, Coyle, & Sharry, 2012; O'Mahen, Grieve, Jones, McGinley, Woodford, & Wilkinson, 2015) and low motivation is a risk factor for dropout (Alfonsson, Olsson, & Hursti, 2016).

Moreover, engaged users have shown improved outcomes after cognitive control training (Siegle et al., 2014). Interestingly, cognitive training has shown increased effectiveness when informing participants beforehand, by manipulating expectations (Long, Hu, Li, Zhang, Yuan, & Chen, 2019). Therefore, the importance of adequate psychoeducation should not be underestimated. A third aspect that COMETS proposed is increasing collaboration over different domains, where larger multinational teams can realize major projects. Lastly, they call for rapid implementation techniques, such as agile design principles, with involvement from the end-users, which allows for improvements throughout a project. Measures for effectiveness and engagement should be included in these steps. Sustainable implementation might require non-traditional collaborations, as creating revenue can be needed to ensure viability and should be thought out early on.

In a follow-up paper, Fleming et al. (2017) stated that using serious games and gamification techniques (i.e., game elements in a non-gaming context) for internet-based interventions are particularly interesting as they might increase impact through three processes: appealing potential, engaging potential and effectiveness potential. First, increasing the reach of interventions decreases the treatment gap and enables affecting more individuals. Second, having more engaging software helps reducing dropout, resulting in better outcomes overall. Third, opportunities for conventional and non-conventional processes for behavior change and learning are provided, where some are based on traditional treatments but this is not necessary.

Thesis Outline

The aim of this thesis is improving and implementing cognitive control training as a preventive measure for remitted depressed individuals, given promising effects in previous research. In accordance with recent calls regarding internet-based treatments, this newly developed cognitive control training should be online, engaging, individualized and cost-

effective, and show similar or increased effectiveness as previous training implementations. Furthermore, this project aims to answer some unanswered questions regarding cognitive control training. For instance, the impact of gamification elements and moderators of effectiveness are currently unknown.

As a first step in creating and implementing an improved cognitive control training intervention, the intended users should be included in the development phase. **Chapter 2** describes a user requirements analysis, based on interactions with remitted depressed individuals and mental health care professionals. Discussing their daily routines, interactions with technology and experiences with a previous cognitive control training version, we identified several possible barriers and facilitators, and mandatory and desirable requirements for this type of cognitive training.

After collecting user input, new software was developed with an external subcontractor. **Chapter 3** describes this software development phase. As a first step, a design document was created that listed all details regarding the new training tool. A second step refers to the actual development of the software, using an agile approach. During this step, provisional software was tested by a small group of remitted depressed individuals. The last part of this chapter exhibits the final software in a visual fashion. Chapter 4, 5 and 6 utilized this newly developed software in their procedures.

As a first empirical validation test of the software, **chapter 4** describes a study with a healthy convenience sample. Contrasting the cognitive control training (n = 74) with an active control condition (n = 73) informed whether cognitive and emotional transfer occurred and how this newly developed training compared to earlier cognitive control training software. Furthermore, gamification was manipulated in both training conditions (low: n = 73 vs. high: n = 74) to increase engagement and monitor unwanted side effects.

The training software was applied to a clinical sample in **chapter 5**. Specifically, a sample of remitted depressed individuals received either cognitive control training (n = 34) or an active control condition (n = 34). The low gamification version was chosen for both conditions and variables were assessed before and after training, and at three and six month follow-up. Depressive symptomatology, rumination, emotion regulation, residual symptomatology, quality of life, resilience, effortful control, and engagement were measured. This study additionally served as a replication and extension study of Hoorelbeke and Koster (2017).

As training effects are not found consistently in all participants, **chapter 6** pertains to finding moderators for cognitive control training effectiveness. Cognitive control training was administered to a large and varied group of self-identified worriers (n = 311). There was no active control condition and the highly gamified task version was used in this study. Participants were assessed before and after training, and after one month. The full protocol was internet-delivered and there was no face-to-face contact.

Chapter 7 discusses the empirical findings and their implications. Additionally, we highlight some of the limitations of the current research and propose future research avenues to further improve the dissemination of cognitive control training.

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Chapter 2: Gamified Cognitive Control Training for Remitted Depressed Individuals: User Requirements Analysis[1]

Abstract

Background: The high incidence and relapse rates of major depressive disorder demand novel treatment options. Standard treatments (psychotherapy, medication) usually do not target cognitive control impairments, although these seem to play a crucial role in achieving stable remission. The urgent need for treatment combined with poor availability of adequate psychological interventions has instigated a shift toward internet interventions. Numerous computerized programs have been developed that can be presented online and offline. However, their uptake and adherence are oftentimes low.

Objective: The aim of this study was to perform a user requirements analysis for an internet-based training targeting cognitive control. This training focuses on ameliorating cognitive control impairments, as these are still present during remission and can be a risk factor for relapse. To facilitate uptake of and adherence to this intervention, a qualitative user requirements analysis was conducted to map mandatory and desirable requirements.

Methods: We conducted a user requirements analysis through a focus group with 5 remitted depressed individuals and individual interviews with 6 mental health care professionals. All qualitative data were transcribed and examined using a thematic analytic approach.

[1] Based on Vervaeke, J., Van Looy, J., Hoorelbeke, K., Baeken, C., & Koster, E. H. W. (2018). Gamified cognitive control training for remitted depressed individuals: user requirements analysis. *JMIR serious games*, *6*(2), e6. https://doi:10.2196/games.8609

Results: Results showed mandatory requirements for the remitted sample in terms of training configuration, technological and personal factors, and desirable requirements regarding knowledge and enjoyment. Furthermore, knowledge and therapeutic benefits were key requirements for therapists.

Conclusions: The identified requirements provide useful information to be integrated in interventions targeting cognitive control in depression.

Keywords: depression, cognitive dysfunction, cognitive remediation, relapse prevention, qualitative research, secondary prevention

Introduction

Background

In 2010, 7.4% of the total worldwide disease burden was attributed to mental and substance use disorders, of which depressive disorders accounted for the most disability-adjusted life years (Whiteford et al., 2013). As such, major depression is recognized as a global leading cause of disability (World Health Organization, 2016). One of the key challenges within this context is that existing treatments frequently fail to achieve stable remission (for an overview, see National Collaborating Centre for Mental Health, 2010). Furthermore, recurrence and relapse rates are estimated to be 54% in the second year after receiving therapy (Vittengl, Clark, Dunn, & Jarrett, 2007), which increases with the number of previous depressive episodes (Beshai, Dobson, Bockting, & Quigley, 2011; Bockting, Spinhoven, Koeter, Wouters, & Schene, 2006). As a result, preventing recurrent major depression is of paramount importance.

In this context, research suggests that impairments in cognitive control (e.g., Veiel, 1997; Elliott, 2002; Porter, Bourke, & Gallagher, 2007), which refer to difficulties in executive processes such as shifting, inhibition, and updating of information in working

memory (Miyake, Friedman, Emerson, Witzki, Howerter, & Wager, 2000), place one at an increased risk for recurrence of depressive episodes (e.g., Harvey et al., 2004; Stordal et al., 2004). For instance, research indicates that impaired cognitive control hampers effective emotion regulation and task engagement (Joormann & D'Avanzato, 2010; De Raedt & Koster, 2010). Furthermore, remitted depressed (RMD) individuals are still suffering from these impairments (e.g., Paelecke-Habermann, Pohl, & Leplow, 2005; Baune, Miller, McAfoose, Johnson, Quirk, & Mitchell, 2010), where cognitive control deficits are related to the number of past episodes (Vanderhasselt & De Raedt, 2009). Interestingly, recent evidence suggests that traditional therapies leave these cognitive risk factors for depression unaffected, even when effectively reducing symptoms of depression (Shilyansky et al., 2016). These observations have led to the development of cognitive control training (CCT) for depression.

Improving Cognitive Control

The idea behind CCT is that performing it activates the prefrontal cortex repetitively, which improves attention and cognitive control (for reviews, see Siegle, Ghinassi, & Thase, 2007; Koster, Hoorelbeke, Onraedt, Owens, & Derakshan, 2017). In the past decade, CCT has been used in several studies regarding vulnerability for depression, and results overall seem promising (e.g., Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015; Hoorelbeke, Koster, Demeyer, Loeys, & Vanderhasselt, 2016). CCT has been shown to have additional effects to treatment as usual, in terms of rumination and depressive symptomatology (Siegle et al., 2007). In a 1-year follow-up of this study, CCT also demonstrated long-term potential (Siegle, Price, Jones, Ghinassi, Painter, & Thase, 2014). Other studies showed that CCT in depression is promising in combination with other treatments, for instance, with transcranial direct current stimulation (Segrave, Arnold, Hoy, & Fitzgerald, 2014). Interestingly, there are some studies that have found that stand-alone CCT also has effects on rumination (Hoorelbeke et al., 2015; 2016; Vanderhasselt et al., 2015;

Calkins, McMorran, Siegle, & Otto, 2015) and depressive symptomatology (Brunoni et al., 2014). A recent meta-analysis of computerized cognitive training for depression showed that it has a small to moderate but nevertheless consistent effect on depressive symptomatology and everyday functioning (Motter, Pimontel, Rindskopf, Devanand, Doraiswamy & Sneed, 2016). Moreover, a recent randomized controlled trial (RCT) showed that CCT, compared with an active control condition, is effective in training cognitive performance and yielded significant differences in terms of rumination, depressive symptomatology, and functioning in an RMD sample (Hoorelbeke & Koster, 2017). Importantly, effects remained stable over time (at 3-month follow-up).

Provided the encouraging findings of well-controlled studies using CCT and the potential to reach a wider population of at-risk individuals through Web-based administration, the CCT program needs to be suitable for Web-based administration. The CCT studies presented above used the Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977). In this task, participants hear a stream of digits, with a certain interstimulus interval (ISI). Participants have to calculate the sum of the last 2 digits and click on the corresponding number. In an adaptive variant of the PASAT (aPASAT), the ISI decreases after a certain number of consecutive correct responses and increases after a certain number of consecutive incorrect responses. However, given that the task is not enjoyable, its user experience is problematic (e.g., Tombaugh, 2006). The task is rather monotonous and demanding, and it can be frustrating at the same time (Siegle et al., 2014; Calkins et al., 2015; Holdwick & Wingenfeld, 1999). The second problem with CCT is that participants have to complete several sessions to benefit from the training (i.e., they have to visit the research laboratory, hospital, or Web-based platform multiple times), which can easily lead to dropout in both research contexts and treatment settings. Indeed, dropout numbers in CCT studies can be substantial. In a selection of 10 influential CCT studies (Siegle et al., 2007; Segrave et al.,

2014; Calkins et al., 2015; Brunoni et al., 2014; Hoorelbeke & Koster, 2017; Alvarez, Cortés Sotres, León, Estrella, & Sánchez Sosa, 2008; Naismith et al., 2011; Bowie, Gupta, Holshausen, Jokic, Best, & Milev, 2013; Lohman, Rebok, Spira, Parisi, Gross, & Kueider, 2013; Owens, Koster, & Derakshan, 2013) in the context of depression vulnerability, mean dropout was at least 21%, ranging from 4% to 50%. If we take sample size into account, total dropout was at least 234 participants of 1697 over the 10 studies, hence 13.79%. Fortunately, enhancing treatment credibility shows potential to counter dropout (Alfonsson, Olsson, & Hursti, 2016) and improve treatment effects (Bendelin, Hesser, Dahl, Carlbring, Nelson, & Andersson, 2011). That is, user engagement has been identified as a crucial variable for mobile health apps (Singh et al., 2016) and CCT procedures (Siegle et al., 2014), where increasing user engagement may thus be of paramount importance to increase effects of CCT interventions.

Increasing User Engagement

One of the ways to achieve this is by means of gamification (Hamari, Koivisto, & Sarsa, 2014). *Gamification* refers to the addition of game elements to nongame contexts, such as points, levels, or a narrative. By increasing engagement, users tend to do better at tasks and rate them more fun at the same time (Deterding, 2011). However, gamification can be implemented in various ways. There are a lot of different game features, and each can have a different effect on a different target population. It has been used in interventions for common mental disorders such as depression, but it is unclear which gamification elements act most effectively (Brown, O'Neill, van Woerden, Eslambolchilar, Jones, & John, 2016). Moreover, little is known about game and gamification preferences of RMD individuals. Provided that patient preferences can influence therapy outcomes (e.g., Lin et al., 2005), gamification elements need to be suitable and motivating for RMD individuals. Recently, a call was launched to increase adherence and decrease dropout rates in internet interventions through,

among other things, increasing user engagement and adding gamification elements (Fleming et al., 2016). In addition, CCT should fit within participants' daily routine. To achieve these goals, a user requirements analysis was conducted.

A *user requirements analysis'* goal is to understand the needs and requirements of the intended users (Maguire & Bevan, 2002). Conducting such an analysis can yield several benefits such as improved user satisfaction, increased productivity, and reduced costs for training and support (International Standards Organisation, 1999). According to Robertson and Robertson (2012), there are different kinds of stakeholders to consider in a user requirements analysis. In our case, the intended beneficiaries of training (operational working area) are RMD individuals. Another group of stakeholders are those who might benefit from the training without being directly in contact with it (containing business): mental health care professionals (MHPs), who can play a key role in prescribing and monitoring CCT. This analysis will therefore regard the requirements of these two stakeholder groups.

Aim of the Study

This study is a first step in developing a new intervention targeted at RMD individuals as a relapse prevention program, through CCT. To increase uptake and adherence, a user requirements analysis was considered crucial. The aim of this study was to explore and map the needs and preferences of an RMD sample and an MHP sample. More specifically, we have 4 research questions. Questions 1 and 2 were queries for the RMD population. Questions 3 and 4 were key questions examined in the group of MHPs.

1. What are the mandatory basic requirements to start CCT?
2. How can user engagement and adherence to CCT be optimized?
3. What are mandatory basic requirements to implement CCT in treatment?
4. How can implementation of CCT in treatment be facilitated?

Method

General

To receive feedback regarding the aPASAT and the broader platform, a user requirements analysis was conducted. To this end, we organized a focus group for RMD individuals, seeing that this is a cost-effective method for analyzing user requirements (Maguire, 2003). To best suit the busy schedules of the clinicians, we conducted individual interviews with them. All focus groups and interviews were conducted in Dutch and were semi-structured, based on a topic list (see section Materials). Citations in this paper have been translated as literally as possible. Names have been changed to guarantee anonymity.

Participants

Remitted depressed individuals. Five participants were included in this focus group. The sample consisted of three men and two women, and their ages ranged from 32 to 62 years (mean 48.4, SD 9.9). All had suffered from at least two depressive episodes in the past and were in remission at the time of the focus group. Three participants (one woman) also participated in an RCT study regarding CCT in the previous year (Hoorelbeke & Koster, 2017) and were selected as part of a follow-up from a larger sample pool. In addition, an organization for patients with depression was contacted through e-mail and yielded the other two participants with no experience regarding CCT. All participants indicated to have a moderate to high affinity for technology as measured by the short version of the Affinity for Technology Scale (ATS; Edison & Geissler, 2003; Geissler & Edison, 2005). They were rewarded with 25 euros.

Mental health care professionals. Six MHPs agreed to be interviewed. All received a psychology degree from a Belgian university. Mean age was 36.7 years (SD 13.1) and ranged between 26 and 65 years. Of the six experts, two were female. Three participants worked as

psychologists, one had recently retired but used to work as a psychologist, one was a researcher who also works as a psychologist with patients, and one was a researcher specialized in electronic and mobile apps for mental health care. The last two held a doctoral degree. All participants indicated to have a moderate to high affinity for technology as measured by the short version of the ATS. Participants were recruited via e-mail. We focused on contacting therapists using a cognitive (behavioral) approach, as well as recruiting professionals from different working environments (e.g., hospital, private practice, and mental health centers). Participants received an incentive of 15 euros.

Materials

Both the focus group and the interviews were recorded on two audio recorders, placed at different locations on the table around which everyone was seated. For the aPASAT demo, a standard Dell laptop (Dell Technologies Inc, Round Rock, Texas, USA) running Windows 7 (Microsoft Corporation, Redmond, Washington, USA) was used. The focus group and the interviews had a distinct topic list because these were conducted with different target groups. These lists were created in advance by the first author (JV), based on the research questions, and sent out to two coauthors (JVL and EHWK) for adaptation and approval. These lists were not changed during the focus group or interviews, but the order was flexibly adapted. However, all topics were covered.

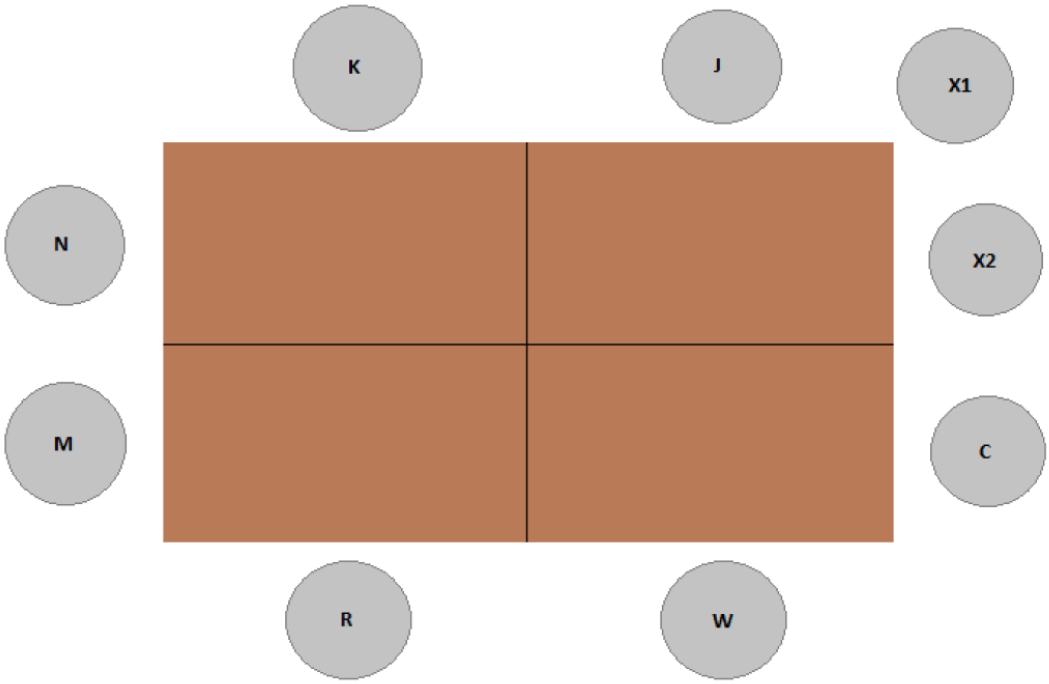
Procedure

Focus group. Participants completed informed consent, a demographic questionnaire, and the ATS. The seating arrangement is illustrated in Figure 1. The focus group included a demo of an aPASAT session that was used in previous studies (e.g., Hoorelbeke & Koster, 2017). At the end of the focus group, participants received their incentive. The whole procedure lasted about 150 minutes and took place at the Faculty of Psychology and

Educational Sciences of Ghent University. The group was moderated by an investigator with extensive experience with focus groups (JVL).

Mental health care professional interviews. Participants completed informed consent, a demographic questionnaire, and the ATS. The interview started with broad, easy-to-answer questions as an icebreaker. After this, the aPASAT demo was presented, and the interview core questions were asked, each followed by probing questions or requests to elaborate. The interviews ended with the incentive. Duration of the interviews ranged from 45 to 90 minutes. Given the busy schedule of interested therapists, the interviews took place at a location of their choice. This resulted in three interviews in the work setting, two at the faculty, and one at home. The interviewer did not have previous interview experience. However, literature regarding interviews was consulted, and two test interviews were conducted with researchers, experienced with interviews.

Figure 1. Seating Arrangement of the Focus Group. Karl (K), Jeff (J), Chris (C), Will (W), and Rachel (R) were participants. M, N, X1, and X2 were moderator, note taker, researcher from the randomized controlled trial (RCT) study, and an employee of a game developer company, respectively.



Data Analysis

All conversations were recorded, transcribed, and analyzed using NVivo (QSR International, Melbourne, Australia), a software package for qualitative data analysis, using an inductive thematic analytic approach (as described in Braun & Clarke, 2006). The coding took place in three broad stages, led by JV, in close collaboration with JVL and EHWK in the third stage. First, transcriptions were given a code as close as possible to the transcription. Here, text segments could have none, one, or multiple codes, and there was overlap between codes. Second, the codes were compared and analyzed. This was done code by code. In this stage, similar codes were merged, and codes with multiple meanings were separated so that each code had only one meaning and a clear coverage that fitted all corresponding text segments. Third, codes were grouped into categories, and different structures were imposed and discussed. Results show the final chosen structure.

Results

General Information

The results are organized in relation to each of the four research questions proposed earlier. Furthermore, each section includes a table that reflects the main findings. Finally, some pitfalls and opportunities are added at the end.

Mandatory Requirements for Remitted Depressed Individuals

Table 1 reflects the mandatory requirements for an RMD sample, which is largely self-explanatory. Patients indicated that a calm and private environment is necessary to focus on the training, but they do not want to feel isolated. Jeff (male, 52 years old, RMD individual) explained how demanding the PASAT can be:

> *When I did the sessions at home, the only time I could complete them was when my children were sleeping and when I asked my girlfriend not to talk for 20 minutes.*

Desirable Requirements for Remitted Depressed Individuals

Features that might help RMD individuals to adhere to CCT are written down in Table 2. Psychoeducation is considered crucial, given that face validity is quite low, and it should emphasize that (1) the main aim of the training is to reduce depressive symptomatology and chances of relapse and (2) the importance of completing the intervention. But when doing so, it should be specific and concrete, as expressed by Rachel (female, 45 years old, RMD individual):

> *I believe you need to be clear, in order to motivate people to keep doing it, to be really clear what it will yield.*

Table 1

Overview of the Mandatory Requirements for the Remitted Depressed Individuals.

Category and subcategory	Requirement	Implementation
Technology		
Functionality	Software works, no bugs, no crashes	Develop bug-free CCT
Usability	Software should be user-friendly	Easy to use; simple text; visually appealing; available on PC and tablet
Person		
Skills	Some internet and technical knowledge	State clear expectations; devise good manual; write clear FAQ section
Access	Internet connection, device in possession	CCT is compatible with most browsers; both on PC and tablet
Configuration		
Time	Not too long and flexible planning of sessions	15 minutes per session; calendar tool to plan next session
Location	Flexible	CCT on an internet website
Setting	Calm and private, but not isolated	Including tablets enables users to complete sessions at preferred location
Pricing	For free	Available for free

Abbreviations: CCT = cognitive control training; PC = personal computer; FAQ = frequently asked questions

Table 2

Overview of the Desirable Requirements for the Remitted Depressed Individuals.

Category and subcategory	Requirement	Implementation
Intrinsic motivation		
Psychoeducation	Knowledge about CCT mechanism and expected outcomes, preferably in an interactive manner	Provide psychoeducation that is clear, simple, and interactive
Practical or technical assistance	Practical and technical guidelines regarding CCT and protocol in case of problems	Devise FAQ section; communicate contact options
Gamification	Training should be enjoyable, engaging, and challenging, by including feedback and reinforcing messages	Include performance-dependent feedback; include performance-independent stimulating messages; individualize CCT
Extrinsic motivation		
Incentivization	Monetary reward after completing all sessions or monetary penalty when dropout	Will not be implemented; available for free
Motivation by therapist	Rationale, follow-up, and encouragement by the therapist when asked for or needed	Therapist will play a role in dissemination and administration, but options not clear at this point

Abbreviations: CCT = cognitive control training; FAQ = frequently asked questions

Participants further agreed that response-related feedback during training is important. This should ideally be clear, instant, and easy to process (in other words, it should not interfere with the ongoing task). Patients reported that in many contexts, feedback is important to improve task performance, whereby improvement itself can be a motivating element in the words of Karl (male, 32 years old, RMD individual):

> *The first session, I was searching. The second one, I was cursing. The third one I was cursing some more, but from the fourth session on, I found it agreeable. Why? Because I noticed I was getting better. So, it is fun, to notice your own progression.*

Another gamification element that patients agreed on was simulated social reinforcement, which can be seen as a kind of reward. Social reinforcement is a form of positive reinforcement and an umbrella term for getting approval from others, by means of attention, praise, and encouragement, among others, as shown in the example of Chris (female, 50 years old, RMD individual):

> *[When playing Candy Crush Saga]…there is a little figure jumping up and down and telling me "Well done!," which I enjoy hearing once in a while. Or you can hear "Sweet!," which I also enjoy hearing.*

The therapist could also play a role in adhering to the training and, more interestingly, this was also offered in the interviews with MHPs; thus, it certainly is considered possible to fulfill this role. Moreover, some MHPs even regarded motivating patients their responsibility, seeing how a therapist's opinion and presentation of a treatment can impact a patient's reception and motivation.

Mandatory Requirements for Mental Health Care Professionals

Table 3 lists the mandatory requirements for a sample of MHPs. As in the previous paragraph with mandatory requirements, this is rather straight-forward.

Desirable Requirements for Mental Health Care Professionals

Features that facilitate implementation of CCT are listed in Table 4. Educating therapists with regard to the training, as well as explaining how and why it works, is considered important for dissemination, especially given the low face validity of this training, as Rudy (male, 65 years old, psychologist) said:

> *When I imagine my colleagues, I think there are certainly some, because they regard it as hocus-pocus, that are not willing to offer it [the training]*.

It might be encouraging to receive training feedback as well as outcomes with regard to depressive complaints, which would allow seeing whether training is effective for specific patients. Therapists indicated that such information could increase motivation to implement training, as Hailey (female, 26 years old, and psychologist) stated:

> *If we, as caregivers, are able to check whether or not they completed a session, or that you [the researchers] would be able to send us a message, for instance "We noticed that this person is not really strict with completing the sessions," we might be able to call that person and really motivate [him/her], like, "Really try to do it anyway" and explain again why exactly it is a good idea.*

In the example above, it is also clear that MHPs are willing to take on a motivational role, as discussed in the previous section.

Table 3

Overview of the Mandatory Requirements for Mental Health Care Professionals.

Category and subcategory	Requirement	Implementation
Permission	Need permission from supervisor or MHP	Get approval by showing scientific evidence; giving psychoeducation
Configuration		
Time	Offering training should not be time-consuming	Devise training to be minimally time-consuming for MHP
Usage	Be informed about practical information of the training	Provide clear guidelines; practical or technical assistance (e.g., contact person)
Format	Available and shareable training	Freely available website (not CD-ROM or other physical carriers)

Abbreviation: MHP = mental health care professionals

Table 4

Overview of the Desirable Requirements for Mental Health Care Professionals.

Category and subcategory	Requirement	Implementation
Intrinsic motivation		
Psychoeducation	Knowledge about CCT mechanism and expected outcomes	Provide clear psychoeducation; tailor it to the working environment
Therapeutic benefits	CCT is beneficial in preventing or postponing a relapse; without major side effects	Test effectiveness of the CCT extensively; check for side effects
Extrinsic motivation		
Resource access	Having access to scientific papers or clinical tools through the university	Unfortunately not possible to implement
Training feedback	Information about execution, performance, and outcome of the patients they proposed CCT to	Unclear at this point; if possible, grant therapist restricted access to database

Abbreviation: CCT = cognitive control training

Pitfalls

RMD individuals and MHPs raised a number of additional concerns and comments that could be taken into account to prevent problems with the training. We will briefly present seven such concerns. First, the PASAT itself is based on math operations, which can be frustrating for some people, especially when time pressure is added. Second, privacy and data protection is considered important. Third, technological skills will vary where it is important to strike a balance for being easy to operate for novice as well as skilled users. Fourth, the amount of additional work in addition to the training (such as questionnaires) needs to be limited. Fifth, having the training publically available means that nobody gets excluded this way, but this comes with the risk of offering the training to relapsed individuals that will not be helped by the training on its own, resulting in a fail experience, further decreasing this person's mood. Sixth, the effect of the training is the strengthening of cognitive control, which is hard to measure and notice and comes only after multiple training sessions, but users might be focused on their performance which is easily measured and visible. Finally, gamification might lead to extra frustration. Having too many gamification elements within the training, so that it distracts from the task, should be avoided.

Facilitating Factors

Facilitating factors are already existing opportunities which might support the uptake of and adherence to this training. First, depression and relapse rates are high, ensuring our training has a large potential user base. Second, in clinical practice, RMD individuals are requesting preventative programs. There are some relapse prevention programs (e.g., mindfulness-based interventions), but the need for targeted interventions for cognitive vulnerability remains. However, RMD individuals sometimes take initiative themselves. Some of them will play brain training or attention games on their own. Here, it is safe to say that the step to our training would not be huge, and these individuals are motivated to prevent

a relapse. Finally, some therapists still have follow-up sessions with RMD individuals, so offering the training through the therapist might be a useful strategy.

Discussion

Principal Findings

The aim of this study was to conduct a user requirements analysis with RMD individuals and MHPs to take into account their preferences in the next steps of development of Web-based CCT, aimed at relapse prevention in depression. For this purpose, we conducted a focus group with RMD individuals and interviewed MHPs. We performed qualitative analyses on the input provided by these participants. Finally, we identified some hindering and facilitating factors that can influence uptake of and adherence to the training.

For the RMD group, there were several mandatory requirements: the training should be functional and user-friendly and match this group's technological skill and access. Performing the training sessions should also fit within their daily routine. Furthermore, this group desired the training to be engaging. Finally, they can be motivated by knowledge of how training works (i.e., psychoeducation), training progress, gamification elements in the training, external factors, and their therapist.

The MHP group postulated some key requirements as well. Offering the training should be approved by their supervisor or director when they are working in a mental health care center. When they are self-employed or need supervisor approval, scientific arguments and research showing the effectiveness of the training and explaining how the training works are needed. Psychoeducation and feedback about patients' progress can increase the chance that therapists will offer this training.

This study has two main strengths. First, as the endpoint of this project is creating an intervention for RMD individuals, we actually involved these end users, as well as MHPs who are in frequent contact with this population. This is in accordance with a recent call by an international collaboration, called "COMETS" (Collaboration On Maximizing the impact

of E-Therapy and Serious gaming). COMETS was created to increase the uptake and adherence to internet interventions for mental health (Fleming et al., 2016). They plead for a paradigm shift that is built on four pillars: (1) increased focus on users, (2) increased focus on engagement, through gamification or other techniques, (3) more inter-sectoral collaboration, and (4) rapid testing and implementation. In this study, it should be apparent that we tried to comply with the first two pillars. Furthermore, we will also attempt to meet the other two by (1) collaborating with software developers who have more experience with good usability, design, and dissemination; (2) conducting research that tests the training's effectiveness as well as the effect of gamification; and (3) thinking about implementation of the training in the early stages of development. By taking into account all these factors, including the results of this study, we hope to decrease dropout rates of CCT and deliver a widely available Web-based intervention.

A second strength is that our findings are in agreement with literature regarding internet-based cognitive behavior therapy, which adds to the reliability of the findings of this study. For instance, previous research has shown beneficial effects of an intuitive and interactive product (Beattie, Shaw, Kaur, & Kessler, 2009), of reminders and motivational prompts (Donkin & Glozier, 2012), and that presented text should match the individual's reading and computer skill (Gerhards et al., 2011). A study by Rozental and colleagues (2015) showed a decrease in motivation for a Web-based intervention when the amount of mandatory reading was too high, as this was too time-consuming.

Limitations

Nevertheless, this study also has some limitations. First, both target populations were represented by a small sample. Findings can therefore not be easily generalized, but it does give us some specific insights. During the focus group with only five RMD individuals, opinions already diverged greatly. Although relatively few people were included, enrolling

too many people in a focus group might work counterproductive (Maguire, 2003). Furthermore, this study counts as a first step. In subsequent research, user experience and engagement will be monitored in larger samples. The generalizability of this study might be rather low; however, the main aim here was to go into depth, which was not hindered by our final sample size. Given these limited samples, we do not assume saturation has been reached. Nevertheless, we believe that the most crucial aspects have been identified.

As a second limitation, because some of the questioned variables are a matter of personal preference, we did not go into detail about those in this study. For instance, Bartle (1996) identified four player types, that each has their own motivation of why gamers play. Different player types are appealed to different game mechanics. Making the distinction would certainly have offered interesting viewpoints. However, as we are aiming to reach the whole RMD population, instead of specific subgroups, we chose not to include this or other distinctions.

Future Steps

Future steps of this project will be to develop the software of the training and platform, based on the input from the RMD individuals and the MHPs, after which it will be tested in several experiments to ensure that the training is efficacious and can be disseminated. The present requirements analysis is a crucial step in ensuring that the target population will be motivated and engaged to perform the cognitive control program.

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Chapter 3: Software Development

A novel assessment and training platform was designed based on the input of service users and clinicians to optimize cognitive control training. In this project, there was budget for a subcontractor to develop this new training tool, based on previous research and our input. We decided to divide this budget into two phases: creating a design document and the actual development of the software. This chapter will provide a description of the steps we undertook to develop the software of the training and surrounding platform, that will be used in the empirical studies described in the following chapters. An overview of the software is provided as well.

Part 1: Design Document

A design document is a descriptive document, where all details pertaining an electronic software application are written down (for instance content, goal, end-users and their preferences, gamification mechanics, story lines, platforms, programming language, controls, graphical specifications, and server hosting). Creating this before the actual software development helps ensuring a clear goal and unambiguous communication throughout the development process for all partners involved.

Following the Ghent University guidelines and some general principles of the law (equality, non-discrimination, transparency, and principle of proportionality), several developer companies in Flanders, Brussels and the Netherlands received specifications regarding the project and were invited to hand in a proposal. In total, 58 companies were contacted via e-mail or through a contact form on their website when no e-mail address was visible. When both contact options were missing, contact was initiated through Facebook or

LinkedIn. Of those 58, 22 companies replied to our call, but only seven eventually handed in a tender. There was an eighth company that delivered their resume because the larger project was of interest to them, but working on this first phase was not feasible. They were not considered in this step.

We compared all seven applications, and focused on estimated costs, date of delivery of the document, proposed approach, and creativity. Of these seven candidates, one was particularly interesting given that one of their employees obtained a psychology degree and had actual clinical experience (and would be involved in this step). In the end, we decided to go with this company, Bits of Love, for the design document.

The final design document was created by Bits of Love in collaboration with us - via meetings, e-mails, conference and telephone calls - and using input from previous research and the user requirements. This step was estimated to be two months of work, although it actually lasted for a little over seven months, with a kickoff meeting on March 3, 2016 and the final documents delivered to us on October 7, 2016. This design document is available in Dutch at http://bit.do/DesignDocPrevenD and served as a basis for Phase 2.

Part 2: Software Development

Selection of candidates for the development of the actual software, was again in compliance with Ghent University's rules regarding subcontractors and various law principles. As this budget was larger than the one for Phase 1, there were some extra steps involved to ensure compliance. First, again, developer companies in Flanders, Brussels and the Netherlands were contacted, through the same channels. In total, 52 companies were invited, excluding six we considered only during the design document phase, given that these companies did not develop software themselves. Of those 52 invited companies, six handed in a tender and were considered candidates. We compared the tenders based on estimated cost,

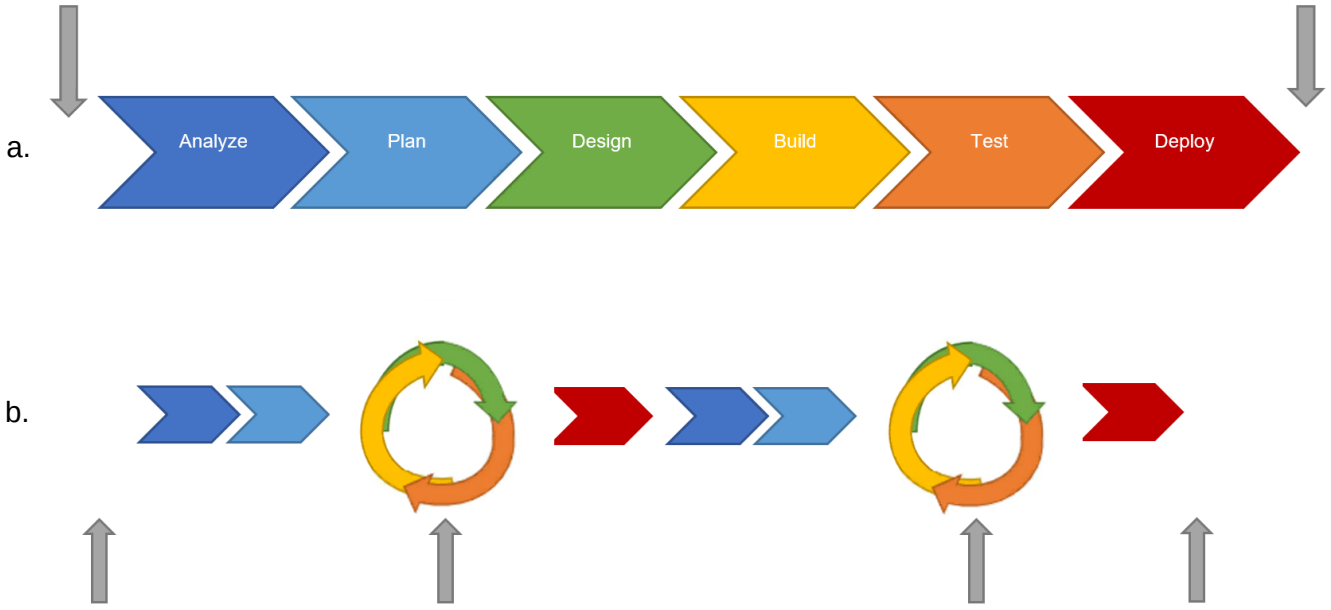
planned duration, creative and technological innovation and creativity of the project, feeling with the target population or any clinical population, scientific affinity, experience with and willingness to collaborate, and transparency regarding data protection, storage and privacy. As a final elimination phase, we selected the two companies that suited our purposes best and invited them for a meeting. Afterwards, the company that would be responsible for the software development of this project was chosen: Bazookas. To conclude the steps that are imposed by Ghent University, a motivated decision letter was addressed to the finances department of Ghent University, elaborating all details regarding the full selection process. A conclusion letter was send out to Bazookas, and the five non-chosen candidates received a non-awarding letter with our motivation.

The software for this project was developed using the agile methodology, instead of the traditional waterfall approach. The waterfall paradigm pertains to a non-iterative process where all software is developed and tested by the developer, without customer involvement during the development phase. Only afterwards, software is presented to the customer. In this model, progress is linear (see Figure 1). In very simple terms, we would send all our input at the start of the project to Bazookas, who would develop the software and deliver it to us when they deem it ready. Several disadvantages have been identified with this approach, such as difficulties with fixing errors afterwards and ambiguous communication between developer and customer leading to different expectations and implementations, resulting in dissatisfied customers. Therefore, a transition to a more agile approach is presenting itself in the software development world. An agile working method includes short iterative cycles throughout the development phase, where parts of the software application are being presented to the customer before progressing to the next one. By doing so, the customer is more involved, problems can be detected earlier and fixed more effectively, and issues in communication

become apparent much more quickly. An example of an agile approach is depicted in Figure 1 but the exact number of iterative loops can differ between projects.

In this project, when a part of the software was finalized, we were able to test it and give feedback using the Zendesk ticketing and bug tracking infrastructure during a predefined period. Beforehand, three such iterative cycles were planned but several more were implemented throughout the development phase. The development phase started with a kickoff meeting on January 30, 2017 and the first tickets were created on February 15. A final meeting with debriefing was scheduled on November 30, 2017, and the last deployment of software was on December 20, 2017. This software development phase took just under a year, which was longer than expected. In the original tender this was estimated to be six months.

Figure 1. Comparison of (a) Waterfall and (b) Agile Approach to Software Development, and Customer Input (depicted with gray arrows).



Part 3: User Testing

As we wanted to involve the target population as much as possible throughout the development of this software, we scheduled a user testing phase with remitted depressed individuals. To this aim, seven remitted depressed individuals came to the Faculty of Psychology and Pedagogical Sciences of Ghent University. Six were participants from an earlier training study and three of them also participated in the focus group during the user requirements phase. Furthermore, the remaining participant was also present during the focus group. Originally, this testing was planned to be at the end of development, but it was shifted to fall within the development phase. By doing so, input from these intended end-users could be integrated in the next stages of development, even though this meant that the software was not fully functional during this testing phase. The intention was that users could navigate the platform freely and using an eye tracker we observed their eye movements. However, given the multitude of bugs still present and diminished functionality of the platform, systematic testing and eye tracking were not possible. Nevertheless, participants received the tutorial videos for the cognitive control and the active control task, and all were able to perform the task without additional support. They reported that the tutorial videos were sufficiently clear to use as stand-alone video tutorials. Overall, participants remarked that this version was an improvement in terms of colors, response button layout and session duration marker (progress bar). Furthermore, with guidance from the researcher present, the aim, structure, and flow of the platform was highlighted as well. Throughout the whole testing session, participants were encouraged to give feedback, ask questions and highlight potential issues. Based on these interactions, several changes were put into the next cycle of software development. For instance, after clicking a response button in a standardized task context (which shows no performance feedback), response-registration feedback is now shown to confirm the response. Furthermore, a short countdown timer before starting a task, in order to prepare participants,

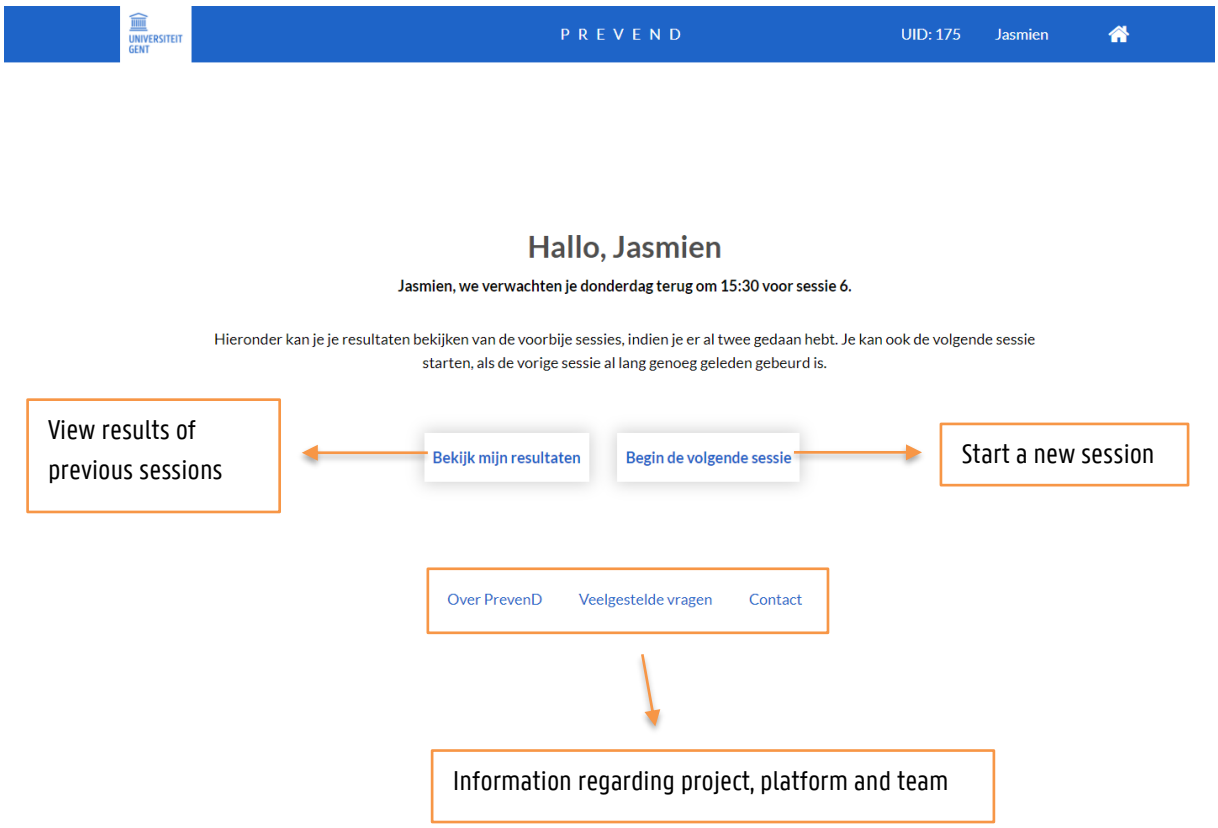
has been included. When the interval to respond has passed (during which new responses are no longer registered), this is also demonstrated in a visible way. A last example regards an adaptation to the scheduling tool for the upcoming sessions, as this was not entirely comprehensible. Additionally, information within text has been altered and/or expanded as deemed necessary by participants. However, it was also requested that the platform should not be text-heavy.

Part 4: Developed Software

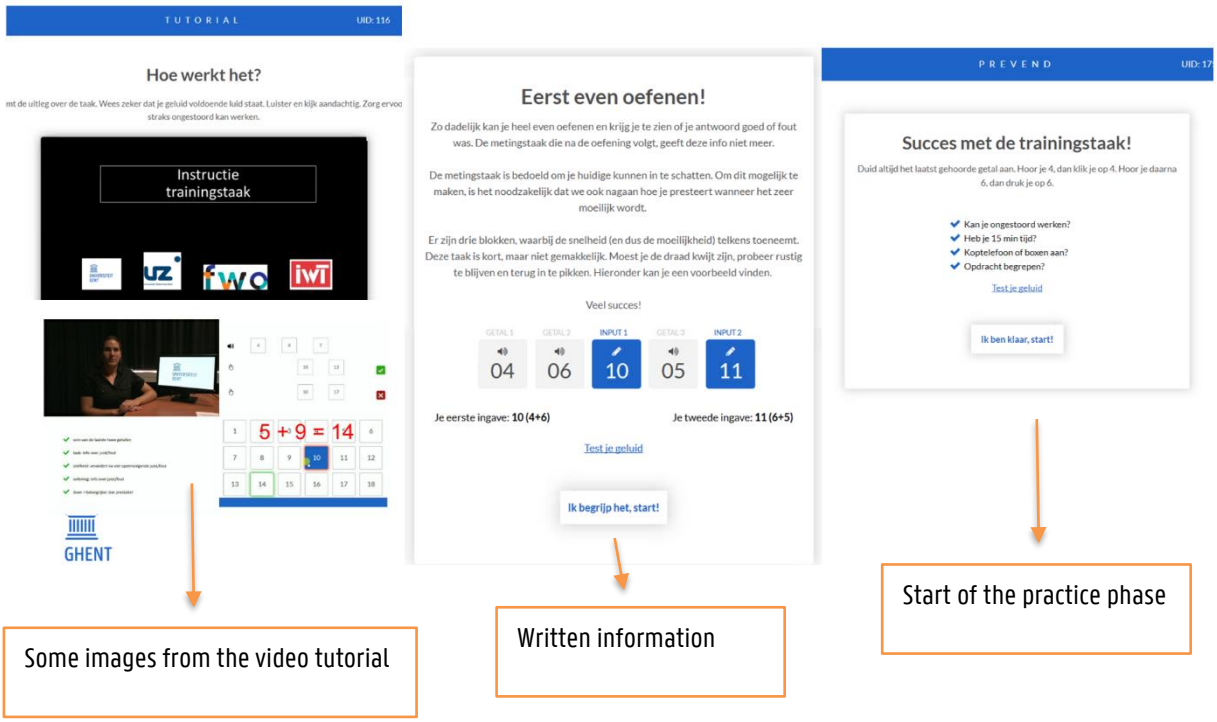
In this final part of this chapter will demonstrate some key features of the developed software using screenshots. However, please note that this does not form an exhaustive overview of the platform. Given that everything is developed in Dutch, some annotations in English are made for clarification in this dissertation. The platform consists of a presentation layer (called front end and is the interface the users see) and a data access layer (or back end for the administrators and researchers).

Front End for Users

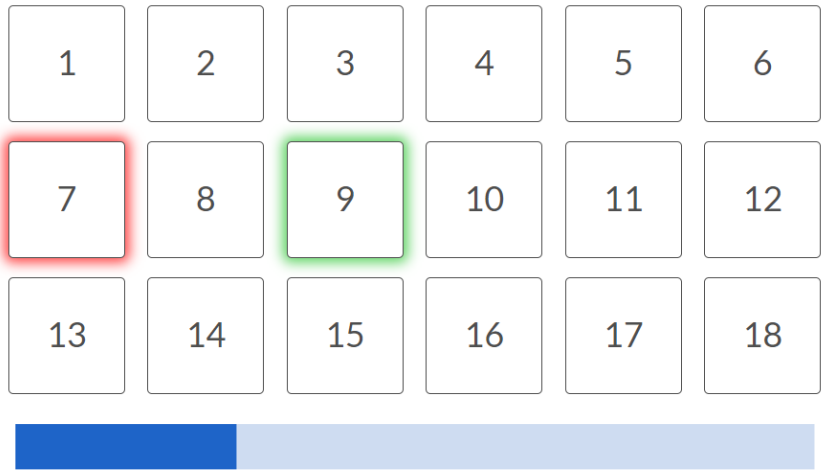
In this platform, all users are assigned an account. After logging in, they can start a new session, or see their progress on past sessions, if applicable. Furthermore, information regarding the platform, the project and the team is always available.



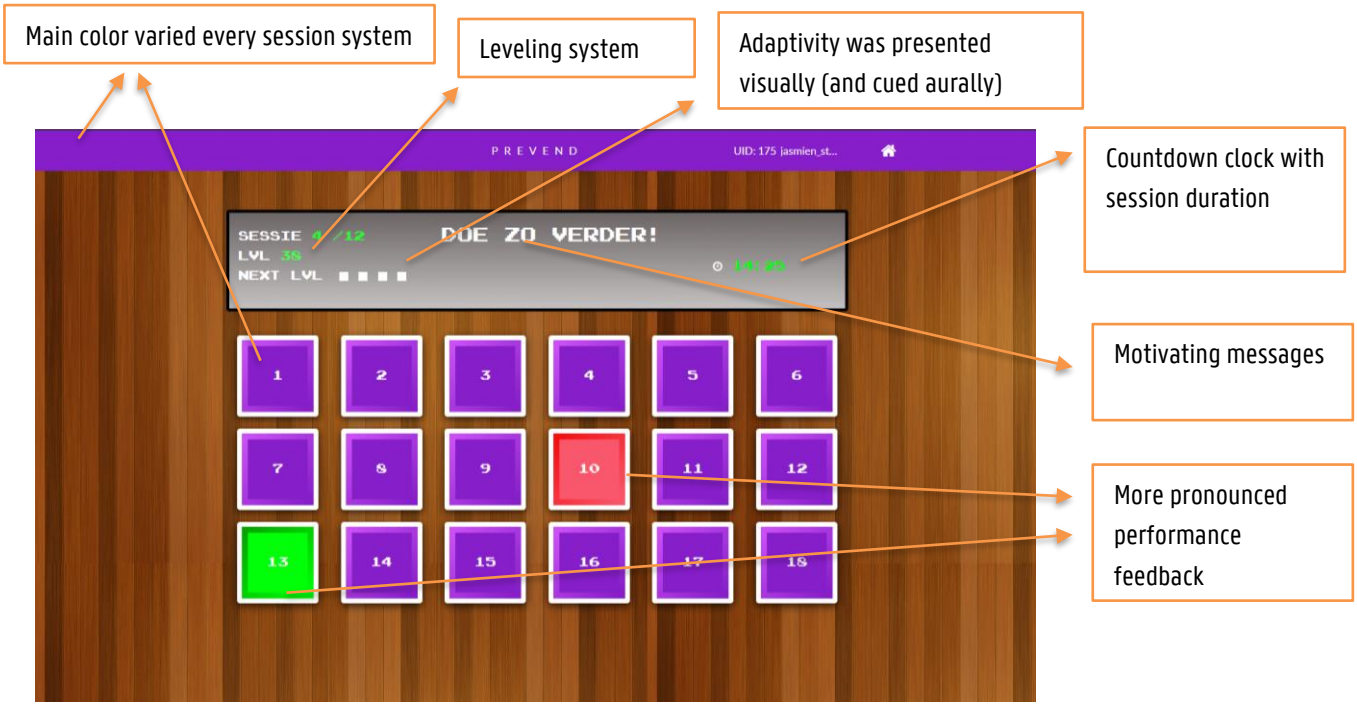
Before encountering a task, either the cognitive control or active control task, a tutorial is shown, consisting of a short video, some written information and a practice phase. An example of a video tutorial can be viewed at http://bit.do/TutorialPrevenD.



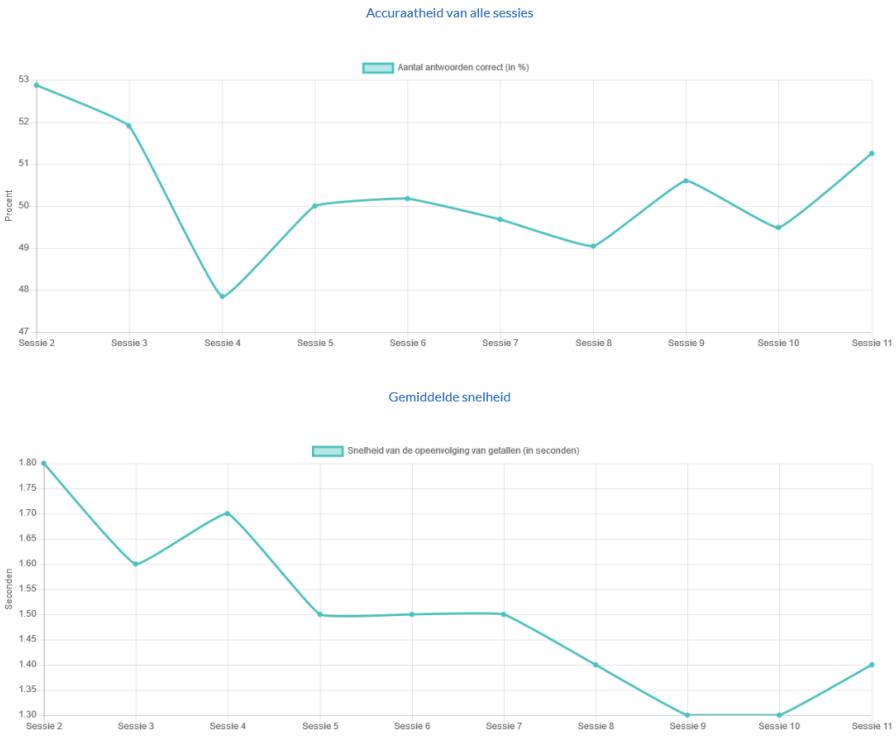
When task instructions are clear, participants can continue with the task itself. Due to the variation in opinions in the requirements analysis, we opted for two task versions: a lightly gamified (upper) and a heavily gamified (bottom) task version. These versions are highly similar, with instructions and task mechanisms being identical. However, some differences are present, aimed at increasing engagement in the highly gamified version. These are explained in full in the next chapter.



Minimalistic design
Performance feedback
Session progress bar
Every session identical



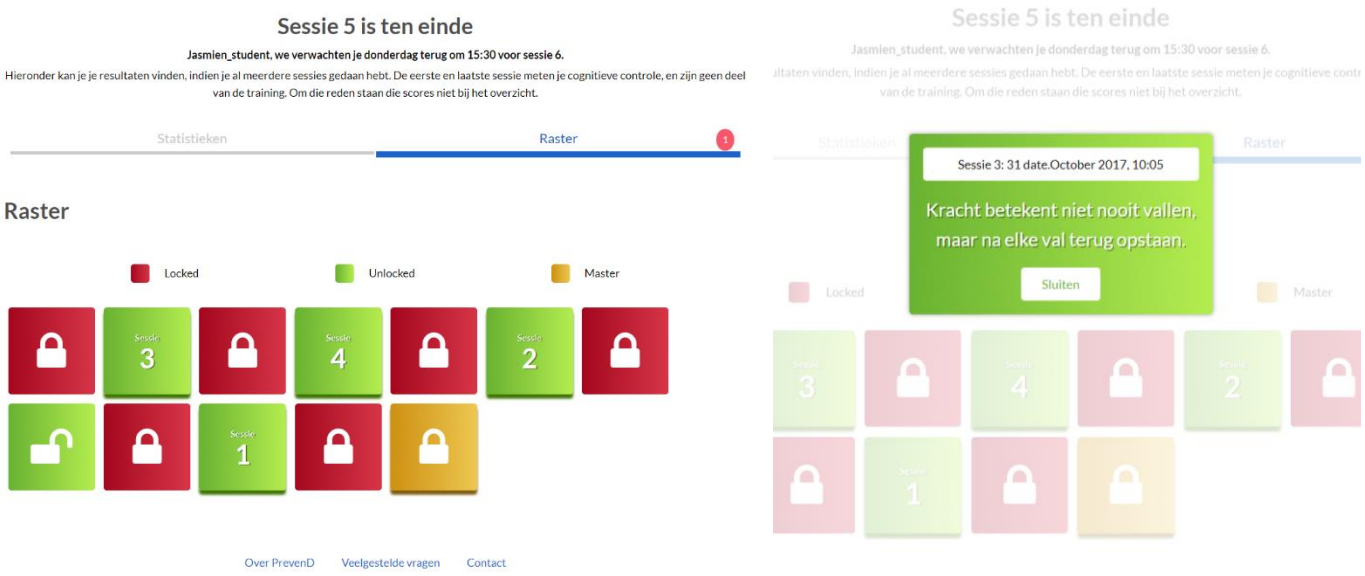
Upon completing the task, performance feedback is presented, in terms of accuracy and speed. In the highly gamified task context, there is an additional graph with points representing a task score, that is based on actual performance, but has a multiplier which increases every training session. This results in increased scores for later sessions, even if objective performance remains equal.



Feedback regarding accuracy over sessions

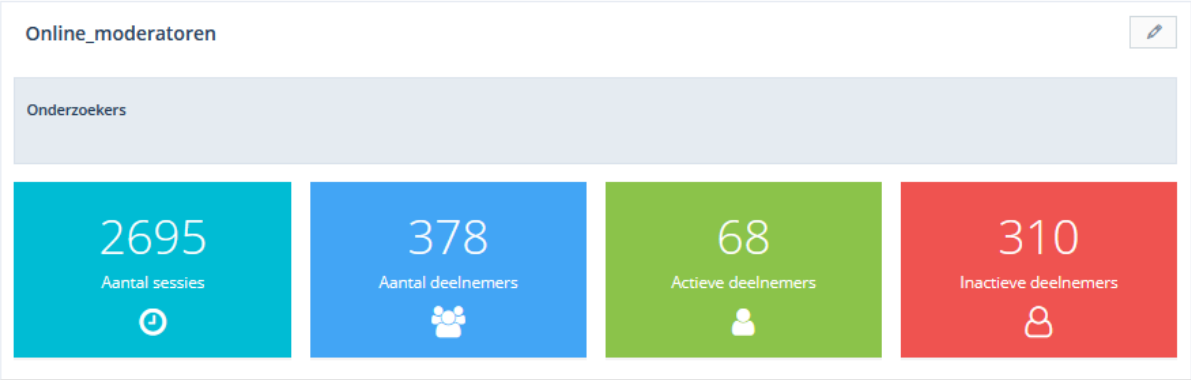
Feedback regarding speed over sessions

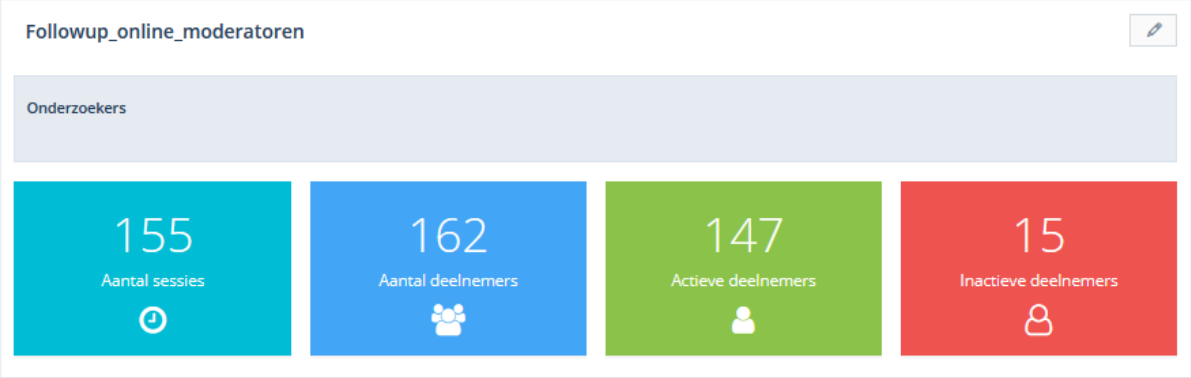
In the highly gamified task context only, there is an additional menu option with a grid. At the start of training, all boxes within in the grid are locked. After finishing a session, one of the boxes randomly becomes unlocked, revealing a quote when interacted with. The number of boxes is equal to the number of sessions, and the final box contains a master quote, from a historical figure.



Back End for Researchers

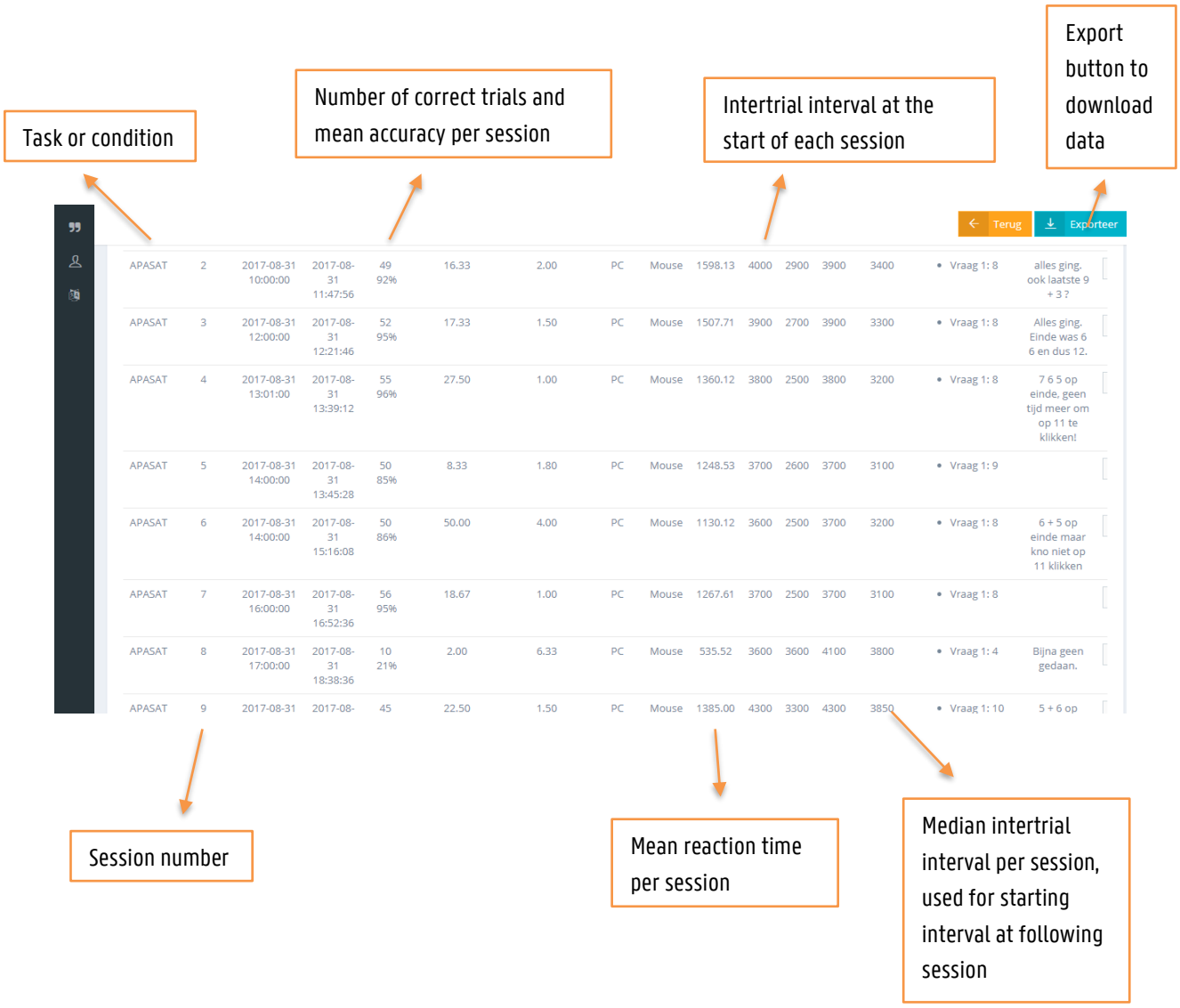
An improvement in this project, compared to earlier training software that was used in our lab, is the data access layer. In this back end, a dashboard is presented with an overview of running studies for easy follow-up.





Furthermore, new training studies can be created with several options. We can choose the number of sessions, conditions, gamification levels, import questionnaires from LimeSurvey, and add psychoeducation per study separately, including optional questions for participants, to make this more interactive.

Lastly, this back end also gives us the possibility to export our data in .csv format. For every participant, we have raw data at trial level where the exact stimuli, accuracy, response time etc. are included, and aggregated data at session level which shows number of trials, overall accuracy, median speed per session as shown in the screenshot below.



Chapter 4: Transfer and Motivation After Cognitive Control Training for Remitted Depression in a Healthy Sample[1]

Abstract

Given that cognitive control deficits following remission from depression form a risk factor for recurrence, new interventions aimed at improving cognitive control such as cognitive control training are being developed. Previous studies suggest that motivation and engagement can influence the effectiveness of cognitive training. As such, we developed a gamified cognitive control training procedure. Before validating this tool in a clinical sample, a convenience sample was used to ensure that gamification did not add any unwanted side effects to the cognitive training procedure. This study was pre-registered on the Open Science Framework (osf.io/5yacs). Following a baseline assessment, participants were assigned to one of four training conditions, manipulating training task (cognitive control vs. active control) and gamification level (low vs. high). Having performed 10 sessions, participants were invited for a post-training assessment. The impact of gamification on cognitive transfer, motivation, and emotional transfer was investigated. Our results suggest task-specific cognitive transfer. In line with our hypotheses, gamification level did not affect cognitive transfer while beneficially impacting motivation. Moreover, beneficial effects of gamified cognitive control training were found for self-reported anxiety levels, in the absence of effects on the other clinical outcomes. This study showed that the newly developed gamified cognitive control training procedure yields similar effects as non-gamified cognitive control

[1] Based on Vervaeke, J., Hoorelbeke, K., Baeken, C., Van Looy, J., & Koster, E. H. W. (2019). Transfer and Motivation After Cognitive Control Training for Remitted Depression in Healthy Sample. *Journal of Cognitive Enhancement*, 1-13. https://doi.org/10.1007/s41465-019-00135-6

training. However, the advantage of this newly developed version is that it is more user-friendly, easy-to-use, online, and that its settings maximize user motivation and engagement, potentially enabling a more effective training.

Keywords: internet intervention, relapse prevention, depression, cognitive control training, gamification, transfer, motivation

Introduction

Cognitive remediation (CR) therapy, referring to treatments consisting of systematic exercises for altering neurocognitive abilities (Robertson & Murre, 1999), is recently being applied in affective disorders such as major depressive disorder (MDD) (Bowie, Gupta, Holshausen, Jokic, Best, & Milev, 2013; Porter, Bowie, Jordan, & Malhi, 2013). The underlying idea is that depression is characterized by cognitive deficits (Austin, Ross, Murray, O'Caŕroll, Ebmeier, & Goodwin, 1992), including impaired cognitive control, which frequently remain present following remission from depression (Paelecke-Habermann, Pohl, & Leplow, 2005; Demeyer, De Lissnyder, Koster, & De Raedt, 2012; Levens & Gotlib, 2015). Cognitive control is key for regulating thoughts and goal-directed behavior. Importantly, such deficits may increase cognitive vulnerability for future recurrence of depressive episodes (Gotlib & Joormann, 2010; De Raedt & Koster, 2010), and existing treatments such as antidepressant medication do not seem to target these cognitive deficits directly (Shilyansky, Williams, Gyurak, Harris, Usherwood, & Etkin, 2016). As such, developing methods that may remediate cognitive impairments in MDD presents a crucial next step.

Although individual cognitive control studies in MDD have produced mixed findings, meta-analyses have shown that there is a small but significant beneficial effect of cognitive training on depressive symptoms (Anaya, Aran, Ayuso-Mateos, Wykes, Vieta, & Scott, 2012;

Motter, Pimontel, Rindskopf, Devanand, Doraiswamy, & Sneed, 2016). This indicates that cognitive training is of potential interest in depression because of transfer effects on both cognitive and affective functioning. In the CR literature, cognitive transfer of training is considered imperative to obtaining beneficial effects on clinical outcomes. In the next sections, literature regarding cognitive and emotional transfer effects is discussed. Lastly, the role of motivation and engagement is considered.

Cognitive and Emotional Transfer

Multiple studies have explored the effects of cognitive control training on the indicators of cognitive functioning (e.g., cognitive task performance, referred to as cognitive transfer) and clinical outcomes (emotional transfer).Within cognitive transfer, we can distinguish task-specific and far transfer effects. Task-specific cognitive transfer in the current paper refers to training-related performance changes on a task similar to the training task, whereas far cognitive transfer refers to training-related performance changes on a task dissimilar to the training task. Training studies aimed at improving cognitive control in the context of depression have utilized a wide variety of training parameters (see Koster, Hoorelbeke, Onraedt, Owens, & Derakshan, 2017 for a review). Two training paradigms have been dominantly used in the cognitive control training literature: the n-back task (Kirchner, 1958; Jaeggi et al. 2003; Jaeggi, Buschkuehl, Jonides, & Perrig, 2008) and the Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977).

Although cognitive transfer has been investigated extensively in healthy samples using the n-back paradigm (Kirchner, 1958; Jaeggi et al., 2003), clear transfer effects are oftentimes not found. In particular, demonstrating far cognitive transfer has shown to be a challenging endeavor (Sala, Aksayli, Tatlidil, Tatsumi, Gondo, & Gobet. 2019). In this context, several factors have been raised, among which age (Katz, Jones, Shah, Buschkuehl, & Jaeggi, 2016), personality (Katz et al., 2016; Studer-Luethi, Jaeggi, Buschkuehl, & Perrig, 2012), training or

study parameters (Schwaighofer, Fischer, & Bühner, 2015; Foroughi, Monfort, Paczynski, McKnight, & Greenwood, 2016; Dougherty, Hamovitz, & Tidwell, 2016), and motivation (Katz et al., 2016; Jaeggi, Buschkuehl, Shah, & Jonides, 2014). In addition, n-back training procedures have yielded limited evidence for emotional transfer effects in the context of depression (for a review, see Koster et al., 2017). That is, as to date, emotional transfer effects of the n-back task in the context of depression have only been studied in two studies using a clinical sample. First, Iacoviello et al. (2014) compared an emotional n-back training to a neutral n-back training. Emotional transfer effects—in terms of beneficial effects of training on depressive symptomatology—were strongest in the emotional n-back training group. However, no differential effects of training condition were found on the indicators of cognitive transfer. Given that no active control condition was used, it is impossible to distinguish training effects from effects of time. Furthermore, this study included only 21 participants, which may have resulted in a lack of power. Second, Wanmaker and colleagues (2015) compared a dual n-back training to an active control condition using a larger sample size. Despite of demonstrating cognitive transfer effects on an inhibition task, no emotional transfer effects were obtained.

In contrast, studies using the PASAT-based training procedure have yielded more promising clinical findings. At the same time, however, studies investigating cognitive transfer after PASAT-based training are rather scarce and results are mixed. For instance, in remitted depressed (RMD) individuals, task-specific transfer effects and reduced cognitive complaints have been observed, even at 3 months follow-up (Hoorelbeke & Koster, 2017). Additionally, combining PASAT training with tDCS in a depressed sample improved performance on a two-back task (Segrave, Arnold, Hoy, & Fitzgerald, 2014). Here, it is noteworthy that other studies using the PASAT-based training procedure in both clinical and non-clinical samples provided mixed cognitive transfer effects. For instance, Hoorelbeke and

colleagues (2016) observed a trend for improved performance on a dual n-back task following training compared to an active control condition. However, multiple studies failed to demonstrate cognitive transfer of PASAT training on other far transfer measures (e.g., Westerberg, Brehmer, D'Hondt, Söderman, & Bäckman, 2008; Brehmer, Rieckmann, Bellander, Westerberg, Fischer, & Bäckman, 2011; Calkins & Otto 2013; Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015; Moshier, 2015; Moshier, Molokotos, Stein, & Otto, 2015).

Although little is known regarding the cognitive mechanisms underlying the PASAT training procedure, it has shown some effectiveness in reducing depressive symptoms in both MDD and RMD samples. That is, several studies demonstrated beneficial effects of PASAT-based training on depressive symptomatology (Siegle, Ghinassi, & Thase, 2007; Segrave et al., 2014; Calkins, McMorran, Siegle, & Otto, 2015; Hoorelbeke & Koster, 2017). In addition, PASAT-based training procedures have shown to positively impact emotion regulation processes, where positive effects were observed on depressive rumination (e.g., Siegle, Price, Jones, Ghinassi, Painter, & Thase, 2014; Hoorelbeke & Koster, 2017).

Theories explaining how PASAT and dual n-back training may yield beneficial effects are still largely untested. Nevertheless, it has been posed that both tasks recruit the dorsolateral prefrontal cortex (dual n-back: Owen, McMillan, Laird, & Bullmore, 2005; PASAT: Lazeron, Rombouts, de Sonneville, Barkhof, & Scheltens, 2003), which typically suffers from decreased activation during and after MDD (as inferred from neuropsychological studies such as Austin et al., 1992; Paelecke-Habermann et al., 2005; Demeyer et al., 2012; Levens & Gotlib, 2015, and neuroimaging studies such as Baxter et al., 1989; Bench, Friston, Brown, Scott, Frackowiak, & Dolan, 1992; Drevets, 2000). Interestingly, it has been suggested that inhibition of limbic interference while performing the PASAT is crucial for task performance. That is, the PASAT is known to induce frustration and stress (Tombaugh,

2006; Siegle et al., 2007), whereas the dual n-back task is not known to induce such feelings. This might be an important differentiator between the two tasks and explain why the PASAT has shown more clinical effectiveness in the context of depression. In this view, PASAT-based training procedures may train inhibition of limbic interference, which could lead to increased inhibition of stress and associated thoughts. This may explain why beneficial effects of training were previously observed on depressive rumination (e.g., Siegle et al., 2007; 2014; Hoorelbeke & Koster, 2017). Furthermore, it also explains partially why emotional n-back training has yielded better results than neutral n-back training (Iacoviello et al., 2014).

Given that there is stronger evidence for the clinical efficacy of PASAT-based training than n-back-based training procedures in the context of depression, we will further investigate cognitive and emotional transfer using this task. Furthermore, in line with previous studies that have demonstrated cognitive transfer following PASAT-based training procedures, we will use a non-adaptive PASAT task to evaluate task-specific cognitive transfer effects (e.g., Hoorelbeke & Koster, 2017), whereas far cognitive transfer effects will be assessed using an n-back task (e.g., Segrave et al., 2014; Hoorelbeke et al., 2016).

Motivation, Engagement, and Gamification

One topic receiving little attention in the cognitive control training literature is engagement and motivation, which may play a key role, given that training procedures usually consist of several sessions, lasting days, weeks, or months, and that motivation of the participants is crucial for transfer after CR procedures (Baldwin & Ford, 1988; Grossman & Salas, 2011; Baldwin, Ford, & Blume, 2009). Indeed, motivation has been shown to moderate n-back performance (Katz et al., 2016; Jaeggi et al., 2014) and early findings with the PASAT suggest task engagement is key, with engaged patients (as indexed by pupil dilation) ruminating less and showing less need for treatment (Siegle et al., 2014). In this context,

gamification—i.e., adding game elements to non-game contexts (Deterding, Dixon, Khaled, & Nacke, 2011)—may play an important role in the transferability of cognitive training.

Recently, gamification has increasingly been implemented in CR research (for a review, see Lumsden, Edwards, Lawrence, Coyle, & Munafò, 2016) and has shown beneficial effects (Looyestyn, Kernot, Boshoff, Ryan, Edney, & Maher, 2017; Khatib et al., 2011; Thom, Millen, & DiMicco, 2012). However, the desired effects of gamification have been absent in some cases (Trushell & Maitland, 2005; Parish-Morris, Mahajan, Hirsh-Pasek, Golinkoff, & Collins, 2013; Hawkins, Rae, Nesbitt, & Brown, 2013; Katz, Jaeggi, Buschkuehl, Stegman, & Shah, 2014). Particularly regarding CR, gamification often increases motivation but has rarely shown to impact training outcomes (Lumsden et al., 2016; Deveau, Jaeggi, Zordan, Phung, & Seitz, 2015; Mohammed et al., 2017). Moreover, it has been suggested that adding gamification to a training procedure can negatively affect cognitive transfer. For instance, the impact of several gamification elements in n-back training was examined recently (Katz et al., 2014). When task accuracy was presented visually, performance decreased, resulting in reduced cognitive transfer. Gamification was assumed to have distracted from training, causing worse performance and less transfer (Katz et al., 2014).

Although maximizing task engagement seems key to cognitive training procedures, as to date, no PASAT-based training studies have investigated the effects of gamification on cognitive and emotional transfer. As such, before implementing a modified training in a clinical sample, cognitive transfer effects of gamified PASAT training should be explored.

Aim of the Study

The aim of the current study is to examine the impact of gamification on user experience, cognitive transfer, and emotional transfer following adaptive PASAT training. A cognitive control training platform was developed based on a focus group with remitted

depressed patients (Vervaeke, Van Looy, Hoorelbeke, Baeken, & Koster, 2018). Before testing this platform using a clinical sample, it is undergoing several development steps, to test essential features for usability in interventional research, following an experimental medicine approach (Riddle & Science of Behaviour ChangeWorking Group, 2015). Our first aim was to map task-specific and far cognitive transfer effects using a standardized version of the PASAT and a dual n-back task where we predicted finding both task-specific and far cognitive transfer (Hypotheses 1 and 2). In addition, we wanted to ensure that gamifying PASAT-based training did not hinder cognitive transfer. In particular, we hoped to find no differences between the high- and low-gamified training tasks in terms of cognitive transfer effects (Hypothesis 3). In contrast, we expected beneficial effects of gamification on user experience, among which self-reported motivation and engagement (Hypothesis 4). Finally, we explored emotional transfer effects of the (gamified) adaptive PASAT training. However, given that a non-selected convenience sample was used, we did not expect to find emotional transfer (Hypothesis 5).

Method

Design

The study was approved by the local ethical committee and pre-registered on the Open Science Framework (osf.io/5yacs) before data collection. Written informed consent was obtained for all participants. The study comprised three phases: baseline assessment, experimental manipulation, and post-assessment. The experimental manipulation consisted of a 2 (training task: cognitive control vs. active control) by 2 (gamification level: high vs. low gamification) design, resulting in four cognitive training conditions. Baseline and post-assessment were identical for all conditions. The training task was manipulated to measure transfer effects. Gamification level was manipulated to obtain knowledge regarding training

progress and cognitive transfer. Additionally, the study aimed to test how gamification affected user engagement and motivation.

Sample and Data Exclusion

Participants were recruited via a Ghent University research platform, a lab database, and social media. Only native Dutch speakers were eligible, due to the language of the training task. Based on a priori power analysis (see preregistration), 168 participants started the study and were randomly assigned to one of four conditions. The full protocol was completed by 153 participants, losing 15 participants to dropout. Furthermore, six participants failed one or more attention check items while completing baseline or post-training questionnaires and were therefore excluded from analyses, but this did not impact the primary pattern of results[2]. Final sample included 147 participants. There were no pre-existing differences between conditions (see Tables 1 and 2). Mean age was 21.4 years and 74.1% were female, with neither age nor sex differing significantly between conditions (Age: $F(3, 143) = 1.06$; $p = .368$; Sex: $\chi^2(3) = 0.28$; $p = .964$).

Material

Baseline and post-training assessments were run on lab computers with a Windows 7 operating system. Questionnaires and non-adaptive PASAT were administered through a cognitive training platform, developed for this project, on Google Chrome. The training was administered online between baseline and post-training assessment, using the same platform. The dual n-back task was administered with Inquisit Millisecond Web license, on Internet Explorer.

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[2] The results were similar for all analyses except for one. When including these six participants, there was no longer a significant impact of gamification on Expectancy ($F(1, 148) = 3.73$; $p = .055$; $\eta_p^2 = 0.03$).

Table 1

Sample Characteristics per Condition per Assessment

	Baseline				Post			
	CCT (n = 74)		ACT (n = 73)		CCT		ACT	
	Low (n = 36)	High (n = 38)	Low (n = 37)	High (n = 36)	Low	High	Low	High
Cognitive measures								
PASAT acc.	39.1% (11.8)	38.0% (11.5)	38.2% (13.2)	42.3% (9.8)	83.6% (9.7)	84.9% (9.1)	53.6% (15.8)	55.7% (10.6)
Dual n-back acc.	1.4 (0.9)	1.2 (1.1)	1.1 (1.2)	1.3 (1.1)	1.7 (1.3)	1.4 (1.3)	1.5 (1.3)	1.6 (1.4)
Emotional measures								
DASS Anxiety	3.4 (4.2)	4.2 (4.8)	6.1 (7.2)	4.8 (4.6)	3.7 (3.4)	3.0 (3.7)	4.8 (5.6)	4.7 (5.2)
DASS Depression	5.1 (5.8)	5.7 (6.9)	7.2 (6.4)	5.3 (5.8)	4.7 (5.5)	4.8 (6.1)	6.7 (7.2)	5.0 (5.8)
DASS Stress	8.4 (6.1)	8.6 (7.4)	10.6 (6.8)	8.4 (6.1)	8.8 (5.8)	7.7 (5.6)	10.5 (7.7)	9.2 (6.9)
RRS Total	42.7 (11.7)	42.0 (11.9)	47.0 (11.2)	42.9 (10.7)	41.3 (11.1)	41.9 (12.8)	43.6 (10.9)	40.6 (10.6)
RRS Brooding	10.0 (2.8)	10.3 (3.6)	11.1 (3.1)	10.0 (2.7)	9.3 (2.8)	9.7 (3.6)	10.0 (3.2)	9.4 (2.9)
RRS Reflection	9.3 (3.5)	9.2 (3.4)	10.2 (3.4)	9.3 (3.1)	8.9 (3.2)	9.3 (3.7)	9.3 (3.2)	8.8 (3.4)
ATQ-EC Att. Control	3.6 (0.8)	3.8 (0.8)	3.6 (1.0)	4.0 (1.0)	3.6 (0.8)	3.9 (0.8)	3.5 (1.0)	3.9 (1.0)
ATQ-EC Act. Control	4.2 (0.9)	4.1 (0.8)	4.2 (0.9)	4.2 (1.0)	4.0 (1.0)	4.2 (0.8)	4.1 (1.0)	4.3 (1.0)
ATQ-EC Inh. Control	4.4 (1.0)	4.5 (0.9)	4.3 (0.7)	4.5 (1.0)	4.5 (1.1)	4.4 (0.9)	4.3 (0.8)	4.6 (0.9)
Motivational measures								
CEQ Credibility	0.07 (2.1)	-0.03 (2.3)	-0.02 (2.4)	-0.22 (2.7)	0.6 (2.4)	1.3 (2.4)	-2.1 (2.3)	-0.1 (2.5)
CEQ Expectancy	0.21 (2.3)	0.15 (2.5)	-0.37 (2.3)	-0.12 (2.0)	0.1 (2.5)	0.9 (3.1)	-1.1 (1.9)	-0.1 (2.4)
Placebo Yes:No	6:30	3:35	7:30	8:28	9:27	9:29	20:17	15:21

Displayed values depict means, with standard deviations between parentheses, except for Placebo where the values are absolute numbers. CCT = Cognitive Control Training; ACT = Active Control Training; SD = standard deviation; acc. = accuracy; DASS = Depression Anxiety Stress Scale (Lovibond & Lovibond, 1993; de Beurs, Van Dyck, Marquenie, Lange, & Blonk, 2001); RRS = Ruminative Response Scale (Nolen-Hoeksema, & Morrow, 1991; Treynor, Gonzalez, & Nolen-Hoeksema, 2003); ATQ-EC = Adult Temperament Questionnaire – Effortful Control subscale (Rothbart, Ahadi, & Evans, 2000; Hartman & Majdandžić, 2001); Att. = attentional; Act. = activation; Inh. = inhibitory; CEQ = Credibility/Expectancy Questionnaire (Devilly & Borkovec, 2000)

Table 2

Statistical Tests from Data Collected during Baseline Assessment

Baseline	Statistic	*df* 1,2	*p*
PASAT accuracy (SD)	$F = 1.08$	3,143	.361
Dual n-back accuracy (SD)	$F = 0.41$	3,143	.748
DASS Anxiety (SD)	$F = 1.64$	3,143	.183
DASS Depression (SD)	$F = 0.86$	3,143	.462
DASS Stress (SD)	$F = 0.97$	3,143	.411
RRS Total (SD)	$F = 1.46$	3,143	.229
RRS Brooding (SD)	$F = 0.96$	3,143	.413
RRS Reflection (SD)	$F = 0.69$	3,143	.559
ATQ-EC Att. Control (SD)	$F = 1.63$	3,143	.184
ATQ-EC Act. Control (SD)	$F = 0.16$	3,143	.924
ATQ-EC Inh. Control (SD)	$F = 0.23$	3,143	.875
CEQ Credibility (SD)	$F = 0.09$	3,143	.965
CEQ Expectancy (SD)	$F = 0.50$	3,143	.685
Placebo Yes:No	$\chi^2 = 3.08$	3	0.380

PASAT = Paced Auditory Serial Addition Task (Gronwall, 1977), SD = standard deviation, DASS = Depression Anxiety Stress Scale (Lovibond & Lovibond, 1995; de Beurs et al,. 2001), RRS = Ruminative Response Scale (Nolen-Hoeksema & Morrow, 1991; Treynor et al., 2003), ATQ-EC = Adult Temperament Questionnaire – Effortful Control subscale (Rothbart et al., 2000, Hartman & Rothbart, 2001), Att. = attentional, Act. = activation, Inh. = inhibitory, CEQ = Credibility/Expectancy Questionnaire (Devilly & Borkovec, 2000)

Training tasks. The experimental manipulation comprised a two-week cognitive training procedure which differed in task content (cognitive control training vs. active control training) and gamification level (low vs. high). Participants completed ten sessions (15 minutes each) of the assigned task.

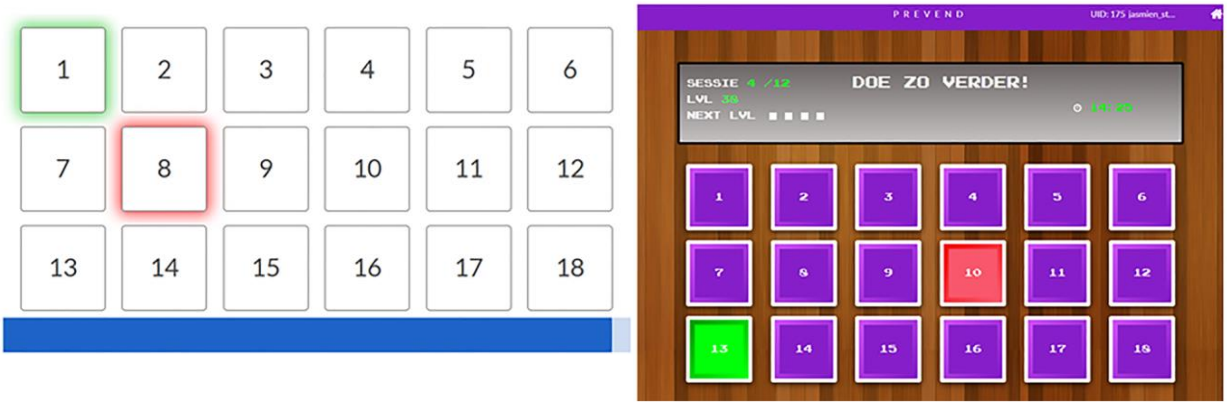
The cognitive control training (CCT) task consisted of an adaptive version of the PASAT. During this task, a continuous stream of digits (1–9) was presented and participants had to click the sum of the last two heard digits on a trial-by-trial basis. Cognitive control was trained using an adaptive intertrial interval (ITI): every four consecutive correct responses,

the ITI shortened by 100 ms, and following four consecutive incorrect responses, the ITI increased by 100 ms. In addition, each session started with an ITI 500 ms longer than the median ITI of the previous session.

Participants receiving active control training (ACT) performed 10 sessions of a low-cognitive load modification of the adaptive PASAT (Hoorelbeke et al., 2016). This task was visually identical to the CCT task, but instructions differed. Participants heard numbers (1–18) and had to click on the corresponding number (speed-of-response training). This task used the same principles of adaptivity, affecting task difficulty within each session and over multiple sessions.

Each of these training tasks existed in two versions: lightly and heavily gamified. For clarity, these will be referred to as low vs. high gamification. The two versions were kept as similar as possible except for gamification elements so that training instructions and mechanisms were identical. Screenshots of both task versions are presented in Figure 1. In the high gamification condition, several elements were added in order to foster a positive user experience, potentially impacting engagement. Visually, the task contained more color(s) and elements, resulting in a more vivid look. The main color theme also varied randomly per training session. Furthermore, session progress was illustrated by a bar in the low gamification version, whereas a countdown timer was presented in the high gamification version. In addition, the high gamification version contained motivating messages. These were provided regardless of actual performance in order to foster task engagement and acted as simulated social feedback. The training level was made visible and increased whenever the ITI did, reinforcing the efforts of participants. In both conditions, there was an identical adaptive component, meaning that the pace increased or decreased after four consecutive correct or incorrect responses. While this was not visualized in the low gamification condition, it was in the high gamification version, along with an auditory cue announcing an

Figure 1. Screenshots of Task Versions for Low (left) and High Gamification (right).



increase in speed. Upon completing a training session, participants in the high gamification version received a session score and were able to compare this with scores of previous sessions, while this was not the case in the low gamification versions. Both versions provided feedback on accuracy and speed. Finally, only in the high gamification versions was there a locked grid at the start of training, in which a cell was unlocked with each session, revealing a motivational quote. Upon completion of the full training procedure (ten sessions), all grid cells were unlocked. Input regarding gamification was collected in a previous stage taking into account the needs and concerns of the users (for a thorough discussion, we refer to Vervaeke et al., 2018).

Cognitive transfer measures. To assess *task-specific transfer* effects of the training procedure, the non-adaptive PASAT (Gronwall, 1977) was administered at baseline and following completion of the training procedure. The non-adaptive PASAT comprised three blocks containing 60 trials each with a fixed ITI (Block 1, 3000 ms; Block 2, 2000 ms; Block 3, 1500 ms), making the task more difficult each consecutive block. The outcome variable was mean accuracy. In this task, participants continuously responded to the sum of each last two heard digits, similarly to the adaptive PASAT, making this a fitting task-specific transfer measure.

The dual n-back task (Jaeggi, Studer-Luethi, Buschkuehl, Su, Jonides, & Perrig, 2010) was used to measure far transfer. This task was used in Hoorelbeke et al. (2016) to measure gains after PASAT-based cognitive training. While the PASAT utilizes primarily attention, processing speed, and working memory (Tombaugh, 2006), the dual n-back task assesses multiple executive functions as well, with little but some overlap in required processes compared to the PASAT (i.e., inhibition of irrelevant items and updating representations in working memory; Jaeggi et al., 2008), making it a well-suited measure of far transfer.

This task used both auditory and visual stimuli. Participants heard one letter from a subset of eight possible consonants. Simultaneously, a blue square was presented visually in one of eight possible locations. Participants indicated whether there was an auditory match, a visual match, or both, with target stimuli presented N trials back (increasing from two to four). Every level of N contained three blocks with 20 target trials. The outcome variable was accuracy, expressed as the proportion of hits minus false alarms, halved, and divided by the number of blocks (Jaeggi et al., 2010). The number of hits and false alarms are absolute values. If there are more hits than false alarms, the outcome value will thus be positive. If the number of false alarms is higher, this value will be negative. Higher outcome values reflect better performance.

Indicators of emotional transfer. As secondary outcome measures, several indicators of emotional transfer were assessed. For this purpose, the following three questionnaires were administered in Dutch at baseline and following two weeks of training: Depression Anxiety Stress Scale (DASS; Lovibond & Lovibond, 1995; de Beurs, Van Dyck, Marquenie, Lange, & Blonk, 2001), Ruminative Response Scale (RRS; Nolen-Hoeksema & Morrow, 1991; Treynor, Gonzalez, & Nolen-Hoeksema, 2003), and the effortful control subscale of the Adult Temperament Questionnaire (ATQ-EC; Rothbart, Ahadi, & Evans, 2000; Hartman & Rothbart, 2001) (see Appendix for more information).

Indicators of motivation. Furthermore, indicators of motivation were included in this study. To check if and how our manipulations impacted the training's credibility, the Credibility/Expectancy Questionnaire (CEQ; Devilly & Borkovec, 2000) was administered at baseline and post-training assessment, alongside an additional item enquiring whether participants believed themselves to be in a placebo condition (similar to Hoorelbeke & Koster, 2017). During post-training assessment, additional questionnaires were administered: the Intrinsic Motivation Inventory (IMI; Ryan, 1982; McAuley, Duncan, & Tammen, 1989) (five subscales: interest/enjoyment, perceived competence, value/usefulness, felt pressure/tension, and effort/importance; the subscales perceived choice and relatedness were left out for brevity and relevance), the Survey to Evaluate Engagement (SEE; Jacques, 1996), and the User Engagement Scale (UES; O'Brien & Toms, 2010) (see Appendix for more information).

Procedure

Baseline assessments started with general and practical information, followed by questionnaires and the non-adaptive PASAT. Next, participants completed the dual n-back task, followed by instructions regarding the training procedure and online training platform. The baseline assessment lasted between 50 and 60 min.

The training itself comprised ten sessions of 15 min each. Participants were instructed to complete all sessions within 14 days. Upon completion of the training task, participants could plan their next training session, and e-mail reminders were sent accordingly. Finally, performance feedback was shown.

Post-training assessments were scheduled 11 working days after baseline and started with questionnaires and non-adaptive PASAT, on the same website used for training. Thereafter, the dual n-back task was administered again, followed by debriefing. The post-

training assessment lasted for 45 to 55 min. After completing the full procedure, participants received 40 euros.

Data Analysis

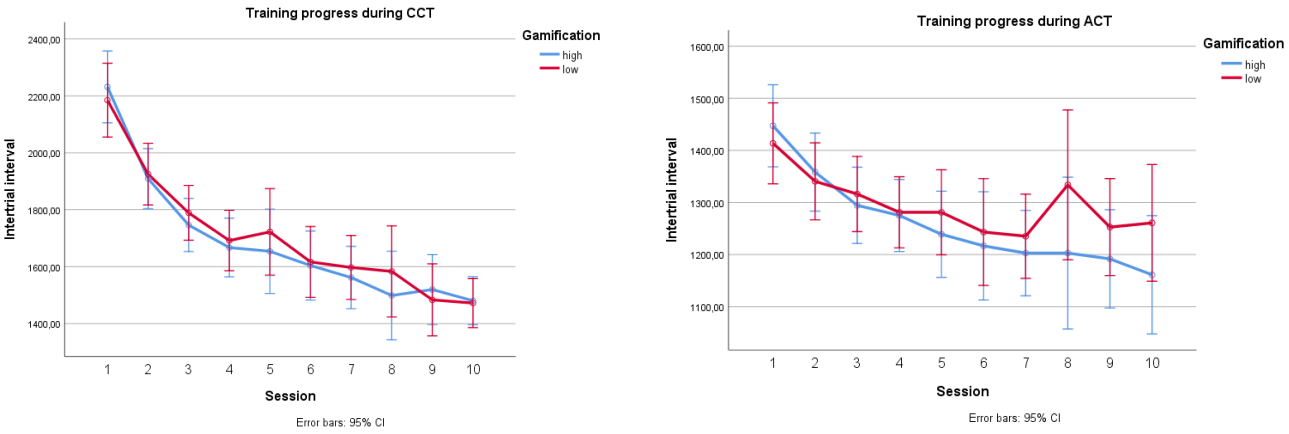
Analyses conducted were in accordance with preregistration. However, for analyses on the pre-post data, ANCOVAs were conducted (with pre-test data as covariates) instead of mixed ANOVAs (see Dimitrov & Rumrill, 2003). Assumptions were checked and when violated, corrected, resulting in adjusted degrees of freedom. For one participant, the post-measurement for the dual n-back task was missing. Consequently, this participant was excluded from analyses involving this task but included for other analyses. Furthermore, due to a technical error in the dual n-back task, visual modality responses were not recorded. Therefore, as an outcome measure, the proportion of hits minus false alarms in the auditory modality, averaged over the number of blocks, was used, as in the single n-back task (Jaeggi et al., 2010).

Results

Training Progression

In line with previous studies (Hoorelbeke et al., 2016; Hoorelbeke & Koster, 2017), training progress was analyzed separately for CCT and ACT due to the different nature of the training tasks. Two mixed ANOVAs were used to map progress during training, measured by median ITIs per session. For each ANOVA, time (ten training sessions) and gamification (low vs. high) were included as within and between-subjects factor, respectively. Results showed significant effects of time for both groups (CCT: $F(4.7, 339.4) = 74.01$; $p < .001$; $\eta_p^2 = 0.50$; ACT: $F(3.8, 271.1) = 11.16$; $p < .001$; $\eta_p^2 = 0.13$), indicating that median ITI decreased over sessions, reflecting improvement on the training task as shown in Figure 2. Importantly, gamification level did not impact training progression. In other words,

Figure 2. Median ITI per Training Session for the CCT (left) and ACT Group (right), for both Gamification Levels.



gamification did not hinder performance on CCT ($F(1, 72) = 0.08$; $p = .783$; $\eta_p^2 < 0.01$) nor ACT ($F(1, 71) = 0.47$; $p = .497$; $\eta_p^2 < 0.01$). Interactions were not significant (CCT: $F(4.6, 333.4) = 0.65$; $p = .651$; $\eta_p^2 < 0.01$; ACT: $F(3.8, 269.3) = 1.50$; $p = .206$; $\eta_p^2 = 0.02$), suggesting that improvements across gamification levels were similar.

Primary Outcome Measures

H1 and H3: Task-specific cognitive transfer and impact of gamification. To examine whether task-specific transfer occurred, a 2 (task: CCT vs. ACT) by 2 (gamification: low vs. high) ANCOVA was conducted on accuracy of the non-adaptive PASAT at post-training assessment. There was a significant effect of training task but not of gamification, after controlling for baseline scores. Furthermore, the training task by gamification interaction was not significant (Table 3).

Follow-up independent samples *t*-tests revealed no difference between training groups at baseline ($t(145) = 0.88$; $p = .38$; $d = 0.14$) and a significant difference during post-assessment ($t(128.3) = 15.49$; $p = .007$; $d = 2.56$). All groups improved from baseline to post-

Table 3

Evidence for Transfer Effects from ANCOVAs[3]

	Effect of Training Task				Effect of Gamification				Task by Gamification Interaction			
Variables	*F*	*df*	*p*	η_p^2	*F*	*df*	*p*	η_p^2	*F*	*df*	*p*	η_p^2
PASAT acc.	**564.55**	**1, 142**	**<.001**	**.799**	0.19	1, 142	.667	<.01	1.35	1, 142	.246	.01
Dual N-back acc.	0.30	1, 141	.588	<.01	0.38	1, 141	.538	< .01	0.03	1, 141	.863	<.01
DASS Anxiety	0.20	1, 142	.652	<.01	0.41	1, 142	.525	<.01	**5.79**	**1, 142**	**.017**	**.04**
DASS Depression	0.52	1, 142	.472	<.01	0.264	1, 142	.608	<.01	<0.01	1, 142	.986	<.01
DASS Stress	1.64	1, 142	.203	.01	0.43	1, 142	.513	<.01	1.23	1, 142	.270	.01
RRS Total	1.36	1, 142	.246	.01	0.26	1, 142	.610	<.01	0.18	1, 142	.674	<.01
RRS Brooding	0.01	1, 142	.936	<.01	0.29	1, 142	.592	<.01	0.01	1, 142	.929	<.01
RRS Reflection	1.01	1, 142	.316	.01	1.04	1, 142	.310	.01	0.17	1, 142	.685	<.01
ATQ-EC Att. C.	0.27	1, 142	.606	<.01	1.75	1, 142	.188	.01	0.42	1, 142	.519	<.01
ATQ-EC Act. C.	0.02	1, 142	.879	<.01	**6.18**	**1, 142**	**.014**	**.04**	0.01	1, 142	.930	<.01
ATQ-EC Inh. C.	0.01	1, 142	.910	<.01	<0.01	1, 142	.982	<.01	2.77	1, 142	.098	.02
CEQ Credibility	**26.6**	**1, 142**	**<.001**	**.16**	**12.4**	**1, 142**	**.001**	**.08**	2.8	1, 142	.094	.02
CEQ Expectancy	**5.4**	**1, 142**	**.022**	**.04**	**5.5**	**1, 142**	**.020**	**.04**	0.01	1, 142	.920	<.01
Placebo (Wald)	**6.2**	**1**	**.013**		1.4	1	.241		0.7	1	.393	

PASAT = Paced Auditory Serial Addition Task (Gronwall, 1977); acc. = accuracy; DASS = Depression Anxiety Stress Scale (Lovibond & Lovibond, 1995; de Beurs et al., 2001); RRS = Ruminative Response Scale (Nolen-Hoeksema & Morrow, 1991; Treynor et al., 2003); ATQ-EC = Adult Temperament Questionnaire – Effortful Control subscale (Rothbart et al., 2000; Hartman & Rothbart, 2001); Att. C. = Attentional Control; Act. C. = Activation Control; Inh. C. = Inhibitory Control; CEQ = Credibility/Expectancy Questionnaire (Devilly & Borkovec, 2000).

[3]: All statistics reported here are based on ANCOVAs, except for the placebo check item (final row in the table) where a binary logistic regression was conducted, resulting in a Wald-statistic.

assessment; however, the CCT group improved more (from 38.6% to 84.3%; compared to ACT: from 40.2% to 54.7%), indicating a task-specific transfer effect of CCT.

H2 and H3: Far cognitive transfer and impact of gamification. To check for far transfer, another 2 × 2 ANCOVA was conducted, using performance on the dual n-back task. Neither training task, gamification, nor their interaction yielded significant effects (Table 3). Hence, there was no evidence for training-related far transfer effects. However, it is possible that participants were performing differently in the visual modality of the task and that transfer occurred there. Due to the data loss in this modality, we will refrain from making strong claims regarding far transfer.

Secondary Outcome Measures

H4: Impact of gamification level on motivation. At baseline, conditions were similar in terms of credibility, expectancy, and belief to be in a placebo condition. At post-assessment however, motivational differences were found (Table 4). Conducting 2 × 2 ANOVAs (Table 5), the post-training scores of the SEE, IMI interest/enjoyment, and perceived competence were significantly higher in the high gamification condition. Furthermore, values for the UES and IMI value/usefulness were marginally higher in this condition. Interestingly, there was no effect of gamification on the IMI effort/importance and felt pressure/tension. None of the interactions were significant. These findings suggest that the gamification manipulation was able to increase motivation and engagement and did not result in one task version to be perceived as more difficult or stressful. However, pre-existing differences are an alternative assertion that might explain these results too (but were absent in terms of credibility and expectancy of the intervention, see Table 2).

Additionally, the scores for IMI value/usefulness were significantly higher in the CCT condition. This might be reflecting that the ACT condition was perceived as less beneficial.

Table 4

Values for Motivational Variables Collected at Post-Training Assessment Only

	CCT		ACT	
	Low	High	Low	High
SEE (SD)	42.7 (8.4)	46.9 (8.2)	40.7 (10.6)	43.4 (8.5)
UES (SD)	87.8 (14.0)	94.4 (16.4)	86.8 (16.3)	89.9 (14.6)
IMI IE (SD)	3.3 (1.1)	3.8 (1.2)	3.0 (1.2)	3.5 (1.0)
IMI PC (SD)	3.2 (1.3)	3.9 (1.4)	3.2 (1.2)	3.7 (1.2)
IMI VU (SD)	3.9 (1.2)	4.1 (1.2)	3.0 (1.2)	3.5 (1.2)
IMI EI (SD)	5.4 (0.8)	5.7 (0.7)	5.4 (1.1)	5.5 (0.7)
IMI PT (SD)	4.2 (1.3)	4.2 (1.2)	4.4 (1.2)	4.1 (1.2)

Table 5

Evidence for Motivational Transfer – Results from ANOVAs at Post-Training Assessment

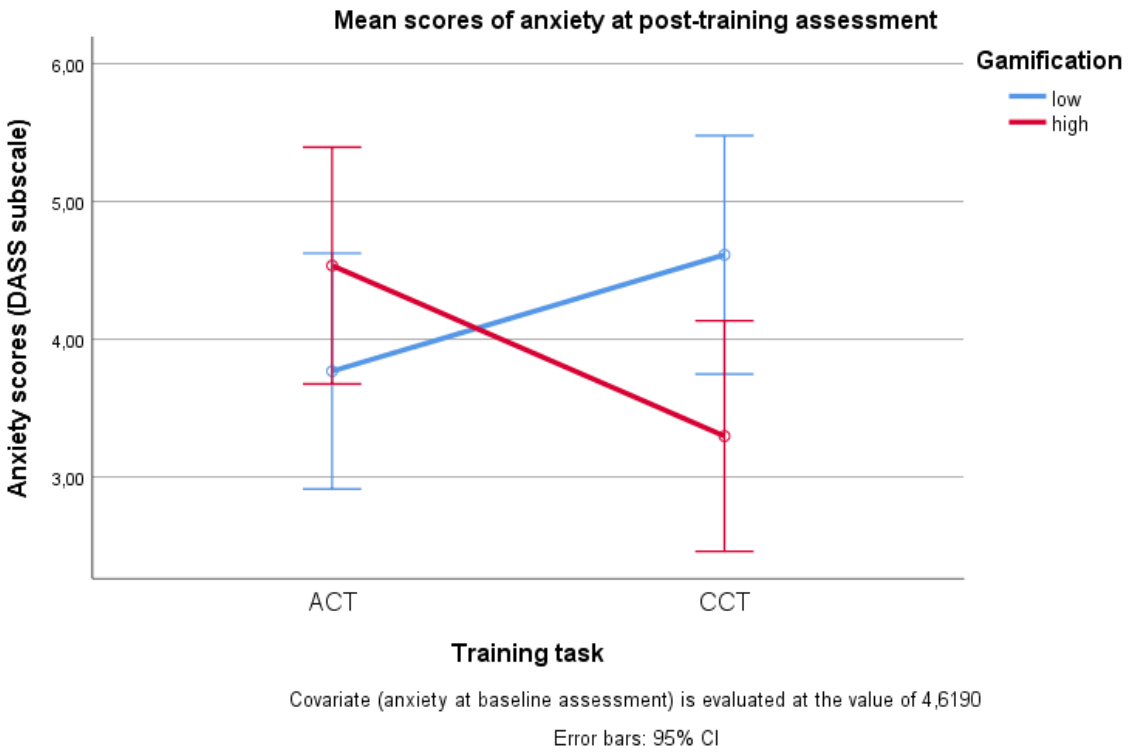
	Main Effect of Training Task				Main Effect of Gamification				Interaction Effect Task x Gamification			
	F	*df*	*p*	η_p^2	*F*	*df*	*p*	η_p^2	*F*	*df*	*p*	η_p^2
SEE	3.42	1, 143	.067	.02	**5.64**	**1, 143**	**.019**	**.04**	0.25	1, 143	.616	< .01
UES	1.17	1, 143	.282	.01	3.70	1, 143	.056	.025	0.49	1, 143	.487	< .01
IMI IE	2.65	1, 143	.106	.02	**7.019**	**1, 143**	**.009**	**.05**	0.10	1, 143	.748	< .01
IMI PC	.15	1, 143	.699	< .01	**9.07**	**1, 143**	**.003**	**.06**	0.27	1, 143	.607	< .01
IMI VU	**15.22**	**1, 143**	**< .001**	**.10**	3.59	1, 143	.060	.03	0.21	1, 143	.647	< .01
IMI EI	.50	1, 143	.482	< .01	1.78	1, 143	.185	.01	0.95	1, 143	.331	.01
IMI PT	0.04	1, 143	.846	< .01	0.22	1, 143	.642	< .01	0.66	1, 143	.420	.01

SEE = Survey to Evaluate Engagement (Jacques, 1996); UES = User Engagement Scale (O'Brien & Toms, 2010); IMI = Intrinsic Motivation Inventory (Ryan, 1982; McAuley et al., 1989); IE = Interest/Enjoyment; PC = Perceived Competence; VU = Value/Usefulness; EI = Effort/Importance; PT = Felt Pressure/Tension

This might also explain the findings at post-assessment regarding the CEQ and the placebo check item. Two 2 × 2 ANCOVAs revealed a significant effect of training task and gamification on the post-scores of the two CEQ subscales (Table 3) but no interaction. Follow-up independent samples *t*-tests showed higher scores for high gamification conditions and CCT conditions, where all differences were significant (CEQ Credibility: training task: $t(145) = 4.96$; $p < .001$; $d = .82$; gamification: $t(145) = 3.14$; $p = .002$; $d = 0.52$; CEQ Expectancy: training task: $t(136.7) = 2.60$; $p = .010$; $d = 0.43$; gamification: $t(140.0) = 2.16$; $p = .033$; $d = 0.36$). A binary logistic regression showed that training task helped predict participants' response on the placebo check item, while gamification did not (Table 3). Participants in the ACT condition were 3.7 times more likely to report believing to be in a placebo condition.

H5: Emotional transfer. Emotional transfer effects were assessed using 2 × 2 ANCOVAs (Table 3). There was a main effect of gamification on the attentional control component of the ATQ-EC, indicating higher scores in the high gamification conditions. The training task by gamification interaction was significant for the anxiety component of the DASS. Post hoc testing revealed significant differences, while controlling for baseline scores. In the CCT group, high gamified training led to lower anxiety scores ($F(1, 142) = 4.69$; $p = .032$; $\eta_p^2 = 0.03$), while this was not the case in the ACT group ($F(1, 142) = 1.56$; $p = .213$; $\eta_p^2 = 0.01$). Additionally, within the high gamification group, CCT led to lower anxiety scores than ACT ($F(1, 142) = 4.16$; $p = .043$; $\eta_p^2 = 0.03$), and this difference was absent in the low gamification conditions ($F(1, 142) = 1.85$; $p = .176$; $\eta_p^2 = 0.01$). Although this seems to indicate that some emotional transfer occurred, estimates of effect sizes were small and there was substantial variability (Figure 3). All other analyses regarding emotional transfer were non-significant.

Figure 3. Mean Scores of Anxiety at Post-Training Assessment, with Confidence Intervals.



Dropout analysis. Of the 168 participants that completed the baseline assessment, 15 dropped out. Out of those 15, two did not start the training. The remaining 13 participants were divided evenly over conditions, suggesting no significant differences of low vs. high gamification on dropout rates ($\chi^2(1) = 0.008$; $p = .685$).

Discussion

This study examined the impact of a gamified PASAT-based training procedure on task-specific and far cognitive transfer, user experience, and emotional transfer, in a healthy sample. Our aim was to ensure that gamification did not impair cognitive transfer while increasing motivation, before implementing training in a clinical context. Training task (CCT vs. active control condition) and gamification level (low vs. high) were manipulated, resulting in four between-subjects conditions. We found that, irrespective of training task or gamification level, participants improved during training. Furthermore, in the CCT condition, there was clear evidence for task-specific cognitive transfer. Far transfer did not appear to occur, but due to partial data loss, this cannot be confirmed or denied using the available data. The motivation and engagement scores were higher in the high gamification version of the training task, while performance was not affected. However, no effects of gamification were observed with regard to dropout. Lastly, as expected for a healthy sample, no evidence was found for emotional transfer on all measures, except for anxiety scores, which were lower in the highly gamified CCT group in comparison to other groups. These findings are discussed below.

The findings show that CCT elicits a task-specific transfer effect. However, for CCT to be effective in a clinical context, far transfer should also occur. Even if there was no data loss, absence of far transfer effects would have been unsurprising and might have been due to the chosen sample which consisted of healthy individuals (see Sala et al., 2019 for a second-order meta-analysis), with little variation in cognitive control. Sampling from restricted ranges of the total population, for instance students, can bias results due to reduced variability, making effect sizes smaller (Bobko, Roth, & Bobko, 2001; Fritz, Morris, & Richler, 2012). For instance, Hoorelbeke et al. (2016) observed a tendency for improved task performance on the

dual n-back task in a convenience sample following PASAT-based training. However, currently, it is not possible to conclude whether or not far transfer occurred.

Importantly, the gamification manipulation seemed to result in a more positive user experience and higher motivation without altering the transfer effects. As such, there appeared not to be any downsides to including the gamification elements used in the current study. This means that adding this type of gamification might help prevent dropout in this training, without impairing cognitive transfer. In the current sample, we did not observe any direct effects on dropout but this could change when training is applied to the intended users that frequently experience motivational impairments. Emotional transfer was only seen in anxiety scores, as measured with the DASS. Scores were significantly lower at post-training assessment for the highly gamified CCT group compared to other groups, while controlling for baseline scores. This means that implementing gamification elements in CCT might lead to a more effective training, as clinical outcome measures are affected. However, caution with interpretation of this finding is advised since we observed considerable individual variability. None of the other emotional transfer variables showed any effect, as was expected in the current healthy sample.

Overall, the current study is encouraging for implementing gamified CCT in a clinical sample. However, there are some limitations to this study as well. First, due to data loss in the dual n-back task, we cannot interpret the far transfer effects readily. We did not find transfer for the auditory modality. The lack of this effect might mean that the training was simply not effective in terms of cognitive transfer. However, other explanations are viable too. For instance, it might be possible that there was a transfer effect in the visual modality or when considering both modalities. Another possibility might be related to the sample. We chose a healthy convenience sample, with unimpaired cognitive control functions, making improvement less probable. Second, there was limited evidence for emotional transfer. That

is, we only observed improvements in anxiety levels. As such, it might be that the training was not effective. However, if this were the case, transfer to anxiety scores is not likely to occur. Third, participants experienced the training as being unpleasant, frustrating, and stressful. Most completed the protocol merely to receive the incentive. As such, it might be hard to motivate patients to complete all the sessions, as they will not receive a monetary incentive. However, a focus on relapse prevention could be motivating enough for this target population. Therefore, thorough psycho-education will be included.

In conclusion, this study provides an essential preparatory step for gamified CCT. There seems to be similar effects with previous versions, and the gamification did not interfere with training effects. We found no reason not to implement this new version of CCT in at-risk and clinical samples, which forms the next step.

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Appendix - additional information about questionnaires

Emotional transfer questionnaires

Symptoms of depression, anxiety and stress were assessed by the DASS (range 0 - 126). Each subscale consisted of 14 items and has recommended clinical cutoffs. Rumination was measured using the 22-item RRS (range 22 – 88). Five items form the subscale brooding, or maladaptive rumination. Reflection refers to purposeful problem-solving strategies and was assessed through five items. Furthermore, 12 items were depression-related. For both questionnaires, higher scores indicated more symptoms or rumination. Effortful control is defined as the ability to suppress a dominant response and choosing a non-dominant one. This was measured by the subscale ATQ-EC which consisted of attentional control (five items), inhibitory control (seven items) and activation control (seven items), measuring capacity to focus and shift attention, capacity to suppress inappropriate behavior and capacity to perform an action when one wants to avoid this, respectively. Each item was scored between one and seven and for each of the three components, a mean score was calculated.

Cronbach's alphas were calculated for each questionnaire on first administration. All were deemed acceptable: 0.95, 0.90 and 0.80 for the DASS, RRS and the ATQ-EC, respectively. Given the interesting aspects of certain subscales, these were also examined separately: depressive symptomatology (0.93), anxiety (0.87) and stress (0.90) for the DASS, maladaptive brooding (0.73) and reflection (0.78) for the RRS, and attentional control (0.62), activation control (0.68) and inhibitory control (0.62) for the ATQ-EC.

Indicators of motivation

The IMI assessed the subjective experience and we selected five subscales: interest/enjoyment (7 items), perceived competence (6 items), effort/importance (5 items), value/usefulness (7 items) and felt pressure/tension (5 items). Each of the subscales can be used independently and the subscale interest/enjoyment is considered to be a measure of intrinsic motivation. In analyses, subscale averages are used (so each subscale ranges from 1 to 7). The SEE consists of 14 items on a 5-point scale (range 14 – 70) and one optional open-ended item asking for additional comments. It is specifically used for capturing engagement with software, consists of seven attributes: attention, time, motivation, needs, control, attitudes and engagement, and has pre-defined levels of engagement based on the sum. Lastly, the UES also measures engagement, but more specifically in an interactive context and uses sum scores. It contains 31 items (range 31 – 155), divided over 6 factors: focused attention (7 items), perceived usability (8 items), aesthetics (5 items), endurability (5 items), novelty (3 items) and felt involvement (3 items).

Cronbach's alphas were calculated for each motivational questionnaire at post-assessment. All were deemed acceptable: 0.88, 0.86 and 0.87 for the CEQ, SEE and the UES, respectively. As certain subscales are particularly interesting, their reliability was calculated as well. For the IMI, the subscales interest/enjoyment, perceived competence, effort/importance, value/usefulness and felt pressure/tension all had acceptable reliability, even with just a few items: 0.89; 0.92; 0.79; 0.94 and 0.79 respectively.

Chapter 5: Online Cognitive Control Training for Remitted Depressed Individuals: A Replication and Extension Study[1]

Abstract

Remitted depressed (RMD) individuals form a risk group for developing future depressive episodes. Improving cognitive control may reduce the risk to develop novel depressive symptoms, as beneficial effects of such training were demonstrated in RMD individuals (Hoorelbeke & Koster, 2017). The current study attempted to replicate and extend these results. In this randomized controlled trial (ClinicalTrials.gov NCT03278756), 68 RMD individuals were allocated to a cognitive control training or an active control condition, each comprised of 10 homework sessions dispersed over two weeks. Primary outcome measures were depressive symptomatology and rumination. Furthermore, emotion regulation, quality of life, residual symptomatology, resilience, user engagement, effortful control and task-specific transfer were assessed. Assessment took place before and after training and at 3 and 6 month follow-up. Results showed training-related cognitive transfer and limited beneficial effects on depressive symptomatology. Given this partial replication, further research into cognitive control training is needed.

[1] Based on Vervaeke, J., Hoorelbeke, K., Baeken, C., & Koster, E. H. W. (submitted). Online Cognitive Control Training for Remitted Depressed Individuals: A Replication and Extension Study.

Introduction

Cognitive deficits can be troublesome symptoms of a major depressive disorder (e.g., Austin, Ross, Murray, O'Carroll, Ebmeier, & Goodwin, 1992, Austin, Mitchell, & Goodwin, 2001; Porter, Bourke, & Gallagher, 2007; Snyder, 2013), that express themselves as problems with attention and memory, and moreover can lead to problematic psychosocial functioning (e.g., work or study problems). In turn, such problems can further decrease self-esteem and quality of life, causing a downward spiral of cognitive and affective processes. Importantly, these deficits often persist during remission from depression (Chen & Hergert, 2017), for instance reflected by attention and immediate memory problems (Baune, Miller, McAfoose, Johnson, Quirk, & Mitchell, 2010). Indeed, a recent meta-analysis showed that several cognitive impairments remain after successful treatment and worsen with the number of previous depressive episodes (Semkovska et al., 2019). In recent years, several theorists have argued that these deficits are not merely a side effect of major depressive disorder, but might form a risk factor for developing new depressive episodes (Joormann, Yoon, & Zetsche, 2007; Millan et al., 2012). It is argued that diminished activation in the prefrontal cortex, which may reflect cognitive control impairments (Collette & Van der Linden, 2002; Smith & Jonides, 1999), is linked to impaired inhibition of amygdala activity, resulting in prolonged limbic activation relating to cognitive processes such as rumination (Siegle, Steinhauer, Thase, Stenger, & Carter, 2002; De Raedt & Koster, 2010). In this context, cognitive control can be defined as processes responsible for adapting information processing and behavior in line with current goals (Braver, 2012; Koster, Hoorelbeke, Onraedt, Owens, & Derakshan, 2017). Furthermore, cognitive control is negatively associated with depression (Harvey et al., 2004; Moriya & Tanno, 2008; Zetsche & Joormann, 2011; Snyder, 2013; Letkiewicz et al., 2014).

Supporting the view that impaired cognitive control might act as a risk factor for depression, cognitive control deficits have been observed in at-risk groups (e.g., Owens, Koster, & Derakshan, 2011; Levens & Gotlib, 2015), and have shown to predict other emotion regulation difficulties, such as depressive rumination and subsequent depressive symptoms (De Lissnyder, Koster, Goubert, Onraedt, Vanderhasselt, & De Raedt, 2012; Joormann & Gotlib, 2009; Ronold, Joormann, & Hammar, 2018). Furthermore, with every depressive episode, there is an increase in cognitive control deficits (Semkovska et al, 2019) and relapse risk (Beshai, Dobson, Bockting, & Quigley, 2011; Bockting, Spinhoven, Koeter, Wouters, & Schene, 2006). Therefore, there is an increasing interest in interventions that could remediate depression-related cognitive control impairments.

Training Paradigms

In this context, cognitive control training (CCT) may be of particular interest. That is, CCT can be implemented in several ways (e.g., in terms of training paradigm, timing and length of training sessions, number of training sessions; for a review, see Koster et al., 2017). The most frequently used task to this aim is the Paced Auditory Serial Addition Task (PASAT, Gronwall, 1977; Siegle, Ghinassi, & Thase, 2007). In this task, participants hear digits (1-9) and are tasked with indicating the sum of the last two digits, on a trial-by-trial basis. In a standardized, non-adaptive PASAT (naPASAT), multiple blocks with different but fixed intertrial intervals of the digits are presented. In an adaptive PASAT (aPASAT), the intertrial interval is dependent on the performance of the participant and decreases or increases throughout the task. Regardless of version, the PASAT loads on frontal brain regions such as the dorsolateral prefrontal cortex (Lazeron, Rombouts, de Sonneville, Barkhof, & Scheltens, 2003) and relies heavily on working memory, attention and processing speed (for a review, see Tombaugh, 2006). The naPASAT has typically been used to measure cognitive control functioning, while the aPASAT is utilized as a training task, given that

difficulty is set at an adaptive yet challenging individual level (e.g., Siegle et al., 2007; Siegle, Price, Jones, Ghinassi, Painter, & Thase, 2014).

A second, often-used paradigm for CCT is the dual n-back task (Kirchner, 1958; Jaeggi et al., 2003; Jaeggi, Buschkuehl, Jonides, & Perrig, 2008). In this task, participants have to process information in two modalities simultaneously. In most cases, this refers to performing working memory operations on auditorily presented consonants as well as visual input. The aim is to indicate whether the visual and/or auditory stimulus match with the stimuli that were presented *n* trials back. Difficulty of this task can be manipulated by changing the value of *n* on block level, which can be done in a standardized (assessment) or an adaptive (training) manner. The dual n-back task, like the PASAT, recruits the dorsolateral prefrontal cortex (Owen, McMillan, Laird, & Bullmore, 2005).

Modified flanker tasks have also been used in the context of CCT. Participants see a target arrow in the middle, flanked by congruent or incongruent distractor arrows, and respond to its orientation. As incongruent trials call for more cognitive control, manipulating the task to have more incongruent or congruent trials can be used to experimentally manipulate cognitive control requirements (Cohen et al., 2016). A flanker trial followed by a discrimination trial after emotional vs. neutral stimuli, with manipulated contingencies, can serve as training for recruiting cognitive control when processing emotional information (Cohen, Mor, & Henik, 2015).

A final CCT task is based on the negative affective priming task (Tipper, 1985; Joormann, 2004; 2006) and consists of paired trials, where a prime trial is followed by a test trial, unbeknownst to participants. Every trial includes a target and a distractor stimulus and participants need to categorize the target's valence. When the valence of the distractor during a prime trial and target of the subsequent test trial is shared, reaction times on test trials are slowed if inhibition is unimpaired. By altering the valence of the targets and distractors,

participants can be trained to inhibit emotional irrelevant information, and this is posited to decreased brooding (e.g., Daches & Mor, 2014). Other tasks have been used in this context but only rarely (for all tasks, see the overview of Koster et al., 2017).

Research Findings

There has been some evidence for effectiveness of cognitive training for depression. In a meta-analysis by Motter, Pimontel, Rindskopf, Devanand, Doraiswamy and Sneed (2016), small to moderate effects were reported on depressed mood, daily functioning, attention, working memory, and global functioning, but lacking for verbal memory or executive functioning. In terms of clinical outcomes, PASAT-based training seems the most promising where depressive symptomatology has shown to be decreased in multiple studies (e.g., Siegle et al., 2007; Segrave, Arnold, Hoy, & Fitzgerald, 2014; Calkins, McMorran, Siegle, & Otto, 2015) and positive effects on depressive rumination have been found (Siegle et al., 2014; Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015).

In a particularly promising double-blind randomized controlled trial (RCT), Hoorelbeke and Koster (2017) investigated whether applying CCT in a remitted depressed sample could reduce cognitive vulnerability (protocol in Hoorelbeke, Faelens, Behiels, & Koster, 2015). This RCT compared ten sessions of aPASAT with an active control training, over the course of two weeks. Assessments were conducted at baseline, immediately following training, and three months later. Beneficial effects of CCT were found in terms of reduced depressive symptomatology, rumination, residual complaints, and maladaptive emotion regulation strategies. These effects were observed directly after training and were maintained at a three-month follow-up. Interestingly, CCT also had an impact on positive outcomes. That is, the experimental group reported an increase in resilience scores from baseline to three months follow-up, reflecting an overall protective effect of CCT (Hoorelbeke & Koster, 2017). This

demonstrates that PASAT-based CCT holds promise as a preventive intervention for remitted depressed individuals.

While this RCT provided important and clinically relevant information as a first study of effects of CCT in remitted depressed patients, it also has several limitations. First, user experiences were suboptimal. That is, the original training procedure relied on an experimental paradigm that was modified to be conducted online. Assessment of user experiences in a limited subset of the sample indicated that the training procedure could be more engaging (Vervaeke, Van Looy, Hoorelbeke, Baeken, & Koster, 2018). This is particularly noteworthy, as user engagement has been found to be a predictor of CCT effectiveness (Siegle et al., 2014). Second, the original study included a follow-up period of three months, which is commendable. However, follow-up studies exploring effects of CCT over a longer time period are needed to examine the duration of beneficial effects.

Bearing these limitations in mind, we developed a novel CCT platform with end-user involvement, which provides an integrated way to administer questionnaires and present standardized and training tasks, in order to assess participants fully online (for more information regarding the development process, see Vervaeke et al., 2018). The aim of the current study was to conceptually replicate and extend the previous RCT by Hoorelbeke and Koster (2017), using the same methodology, similar measures but a new platform, to assess the stability of the findings. Important novel aspects of our study are the novel online training and assessment platform, inclusion of measures of task engagement, broader measures of psychopathology (e.g., assessment of level of anxiety and stress symptoms, in addition to level of depressive symptoms), and an extended follow-up period.

Based on the findings of Hoorelbeke and Koster (2017), we preregistered the following hypotheses (ClinicalTrials.gov identifier: NCT03278756): Our primary hypothesis is that

CCT will result in a decrease in depressive symptomatology and rumination. Furthermore, we expect maladaptive emotion regulation strategies and residual symptomatology to decrease, while adaptive emotion regulation strategies and quality of life will remain unaffected. Lastly, resilience in the CCT group is thought to show an increase. Given that we also wanted to extend the results, we included effortful control as an outcome, where we expect an increase on the attentional control scale.

Method

Participants

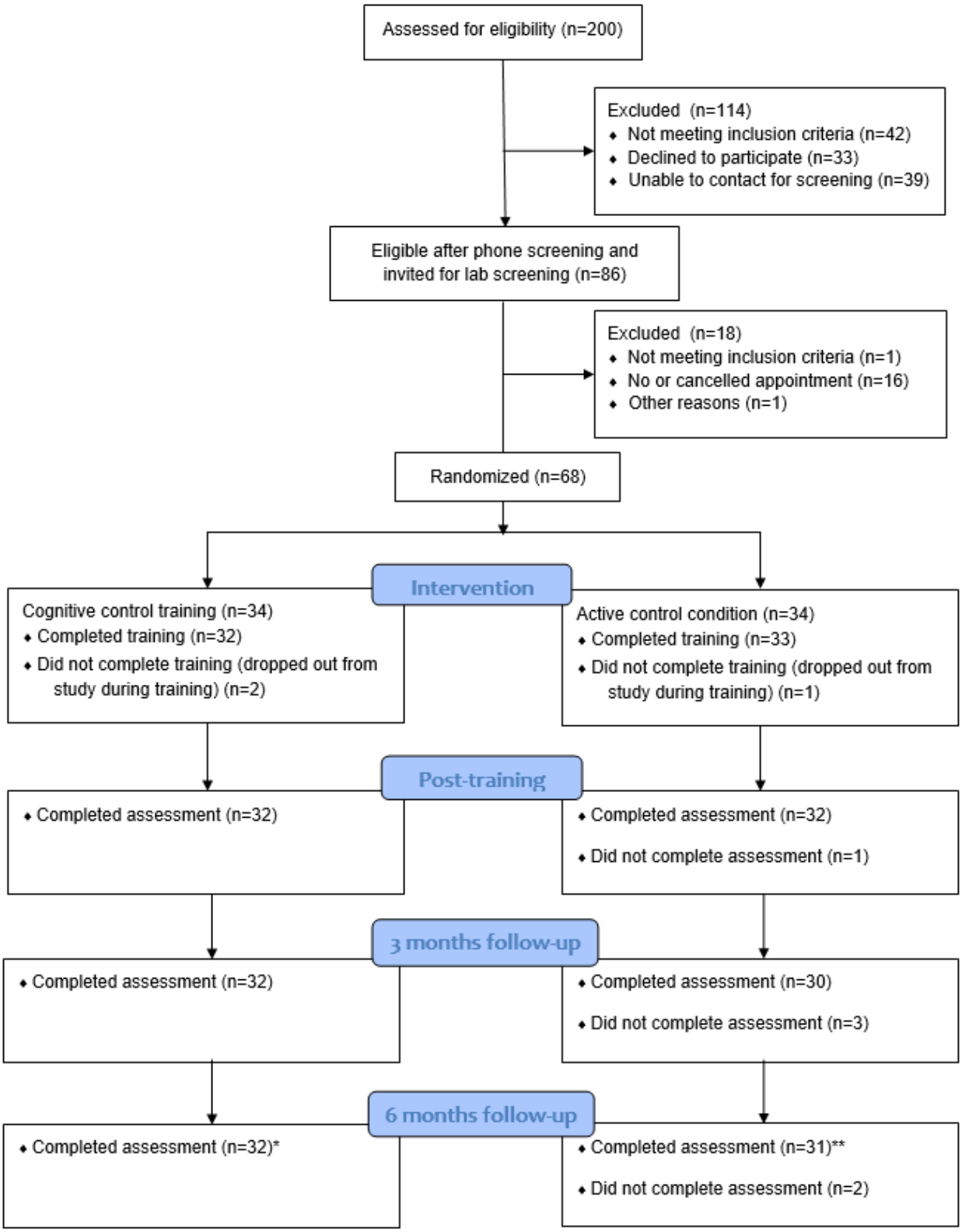
Participants were recruited through media advertisements. In order to be eligible for participation in this study, volunteers had to (a) be between 18 and 65 years old, (b) report a history of depression in absence of an ongoing depressive episode for at least three months, (c) report no history of psychosis, substance abuse or cognitive complaints after brain injury, (d) report using no or a stable dose of medication, (e) report receiving no or stable therapeutic maintenance contact (one session every three weeks, or less), (f) have reliable internet access, and (g) own a functional computer and external mouse or tablet computer. To assess eligibility, a telephone screening was conducted beforehand, where the criteria for current and past depressive episode from the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998; Overbeek, Schruers, & Griez, 1999) were used.

Based on a power analysis conducted for the RCT of Hoorelbeke and Koster (2017; Hoorelbeke, Faelens et al., 2015), 68 participants were enrolled in the study, and randomized to one of two conditions in a double-blind fashion (see Figure 1 for the CONSORT participant flow diagram). Sample characteristics can be found in Table 1. All participants provided written informed consent.

Randomization and Blinding

The random allocation of participants to one of two conditions was performed using the software package RandList, by a researcher that had no contact with participants (KH). By doing so, the researcher in charge of assessing participants (JV) was blind during the phase of data collection. Therefore, all information provided during baseline assessment regarding the training phase and other study steps was identical for the two conditions, ensuring blinded participants. Successful blinding of participants was evaluated at baseline and post-training

Figure 1. The CONSORT Diagram for Participant Flow.



*: Due to a technical error, partial data of 12 participants was lost.

**: Due to a technical error, partial data of 13 participants was lost.

Table 1

Information regarding Demographics and Study Progress, by Condition

	Cognitive control (N=34)	Active control (N=34)	Statistic	df	*p*
Sex (female:male)	20:14	24:10	$\chi^2 = 1.03$	1	.310
Age (SD) *	35.6 (21.6)	44.2 (13.5)	$t = 2.71$	66	.008
Current use of medication no:yes	16:18	13:21	$\chi^2 = 0.54$	1	.462
Current therapeutic contact no:yes	20:14	14:20	$\chi^2 = 2.12$	1	.146
Years in remission (SD)	4.1 (5.1)	2.4 (2.5)	$t = 1.74$	48.1	.088
Number of depressive episodes 1:2:3:4+ *	19:6:5:4	4:9:12:9	$\chi^2 = 15.19$	3	.002
Length of episode(s) in months (SD)	14.8 (13.3)	10.5 (11.5)	$t = 1.43$	66	.157
Number of negative events [LTE] (SD)	1.91 (1.6)	1.65 (1.5)	$t = 0.70$	66	.484
Days from baseline to training (SD)	5.0 (7.4)	3.1 (3.2)	$t = 1.43$	66	.158
Training duration in days (SD)	12.8 (1.8)	12.7 (2.7)	$t = 0.94$	56.5	.926
Days from training to post-assessment (SD)	4.5 (3.1)	4.2 (3.1)	$t = 0.40$	62	.689
Days from training to follow-up 1 (SD)	96.4 (5.6)	94.6 (5.8)	$t = 1.24$	60	.219
Days from training to follow-up 2 (SD)	185.4 (3.9)	184.9 (5.0)	$t = 0.39$	61	.696

*: $p < .05$

assessment with the Credibility/Expectancy Questionnaire (CEQ; Devilly & Borkovec, 2000). In addition, JV remained blind for training condition during the phase of data-analysis. That is, KH provided a list grouping the subjects in two non-informative conditions and data from the primary and secondary outcome measures were analyzed separately from data from the training tasks.

Design

The full study protocol was approved by the medical ethical committee and preregistered on ClinicalTrials.gov (identifier code NCT03278756). It consisted of the following phases: (1) telephone screening, (2) screening and baseline assessment in the lab, (3) training phase, (4) online post-training assessment, (5) online follow-up assessment, and (6) final follow-up assessment in the lab. Except for the training procedure used, all phases were identical for the two conditions. As an experimental manipulation of cognitive control, participants repeatedly completed a cognitive control or active control task. All participants were instructed to start training within two weeks following the baseline assessment (BA), and to complete the post-training assessment (PA) within one week of the last training session. The online follow-up assessment (FU 3M) was scheduled three months after completion of the final training session. The final follow-up lab assessment (FU 6M) took place six months after completion of the training procedure.

Outcome Variables

All questionnaires and tasks were provided in Dutch and administered at every assessment, unless specified otherwise. For a full overview of all variables that were assessed at the different time points, see Table 2. For the primary outcome measures, higher scores reflect more symptoms or maladaptive processes. In terms of secondary outcome measures, this was reversed, with higher scores being indicative of more positive outcomes or adaptive

Table 2

Overview of Variables in the Study Design

	BA	PA	FU 3M	FU 6M
Primary outcomes				
DASS	X	X	X	X
BDI-II	X			X
RRS	X	X	X	X
Secondary outcomes				
CERQ	X	X	X	X
QLDS	X	X	X	X
RDQ	X	X	X	X
CDRS	X	X	X	X
Other outcomes				
LTE	X	X	X	X
CEQ	X	X		
ATQ-EC	X			X
UES		X		
naPASAT	X	X	X	X

BA = baseline assessment; PA = post-training assessment; FU 3M = follow-up at three months; FU 6M = follow-up at six months; DASS = Depression Anxiety Stress Scales; BDI-II = Beck Depressive Inventory II; RRS = Ruminative Response Scale; CERQ = Cognitive Emotion Regulation Questionnaire; QLDS = Quality of Life in Depression Scale; RDQ = Remission from Depression Questionnaire; CDRS = Connor-Davidson Resilience Scale; LTE = List of Threatening Experiences; CEQ = Credibility/Expectancy Questionnaire; ATQ-EC; Effortful Control subscale of the Adult Temperament Questionnaire; UES = User Engagement Scale; naPASAT = non-adaptive Paced Auditory Serial Addition Task

processes, except for the maladaptive emotion regulation strategies and remission from depression.

Primary outcome measures. *Depressive symptomatology* was measured with the Depression Anxiety Stress Scales (DASS; Lovibond & Lovibond, 1995; de Beurs, Van Dyck, Marquenie, Lange, & Blonk, 2001) at every time point, which contains a subscale for depressive, anxiety and stress symptoms (range of each subscale: 0-42). Furthermore, the Beck Depression Inventory – II (BDI-II; range: 0-63; Beck, Steer, & Brown, 1996; Van der Does, 2002) was administered, at BA and FU 6M. *Depressive rumination* was measured during every assessment, with the Ruminative Response Scale (RRS; Nolen-Hoeksema & Morrow, 1991; Treynor, Gonzalez, Nolen-Hoeksema, 2003), which reports rumination (range: 22-88), brooding (range: 5-20) and reflection (range: 5-20).

Secondary outcome measures. *Adaptive and maladaptive emotion regulation strategies* were measured with the Cognitive Emotion Regulation Questionnaire (CERQ; Garnefski, Kraaij, & Spinhoven, 2001). The CERQ contains several subscales, reflecting use of (mal)adaptive emotion regulation strategies. Adaptive strategies include acceptance, taking perspective, planning, positive reappraisal, and positive reflection. Maladaptive strategies contain catastrophizing, ruminating, blaming yourself and blaming others. In line with Hoorelbeke and Koster (2017), we will use compound scores for adaptive and maladaptive emotion regulation strategies (range maladaptive compound score: 16-80; range adaptive compound score: 20-100). *Quality of life* was assessed using the Quality of Life in Depression Scale (QLDS; range: 0-34; Hunt & McKenna, 1992; Tuynman-Qua, de Jonghe, & McKenna, 1997). *Remission from depression* was measured with the Remission of Depression Questionnaire (RDQ; range: 0-82; Peeters, Nicolson, Wichers, & Hacker, 2013; Zimmerman et al., 2013). The RDQ contains seven subscales: depressive symptoms, other symptoms, coping, positive mental health, general functioning, life satisfaction, and sense of well-being

and is a measure for residual symptomatology. *Resilience* was measured by the Connor-Davidson Resilience Scale (CDRS; range: 0-100; Connor & Davidson, 2003).

Other outcome measures. A behavioral measure for *cognitive control* was included as well, by means of a non-adaptive Paced Auditory Serial Addition Task (naPASAT; Gronwall, 1977). This task consisted of three blocks counting 60 trials each. Every block had a fixed intertrial interval (Block 1, 3000 ms; Block 2, 2000 ms; Block 3, 1500 ms), increasing difficulty with each block. Mean accuracy was used as a measure for cognitive control. Participants heard a continuous string of digits (1-9) and had to indicate the sum of the last two digits on a trial-by-trial basis. *Effortful control*, as measured by the subscale of the Adult Temperament Questionnaires (EC-ATQ; Rothbart, Ahadi, & Evans, 2000; Hartman & Rothbart, 2001) was assessed at BA and FU 6M. This scale counts three components (range of each component: 1-7): attentional control, activation control, and inhibitory control and acts as a subjective indicator of cognitive functioning.

Control variables. To control for motivational differences, the User Engagement Scale (UES) and Credibility and Expectancy Questionnaire (CEQ) were administered. *User engagement* was assessed using the UES (range: 31-155; O'Brien & Toms, 2010) at PA only. This questionnaire contains six components: aesthetics, endurability, focused attention, involvement, novelty and usability. The CEQ (Devilly & Borkovec, 2000) was administered at BA and PA. This questionnaire measures *credibility and expectancy* separately. *The occurrence of stressful life events* was monitored using the List of Threatening Experiences (LTE; Brugha & Cragg, 1990; Rosmalen, Bos, & de Jonghe, 2012), allowing to control for negative events during the study that might impact outcomes.

Procedure

Screening phase. As a first step, potential eligible participants completed a telephone screening. At this stage, participants received information regarding the study design. Upon confirming interest in participation, eligibility was assessed. (e.g., age, depressive history, current treatment plan, access to technological devices). In particular, we relied on the mood disorders module of the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998; Overbeek et al., 1999). Furthermore, screening questions were asked to exclude candidates with a history of substance abuse, psychosis and cognitive complaints after brain injury. When all criteria were met, an appointment for a second screening and subsequent BA was scheduled.

The second, more elaborate screening took place in the lab, which contained the Dutch Mini-International Neuropsychiatric Interview screening version (Sheehan et al., 1998; Overbeek et al., 1999) for depression (again current and lifetime), suicidal risk, mania, alcohol and substance dependence/abuse (modules A, C, D, J and K, respectively). Whenever a screening question received a positive response, the full corresponding module was administered. The module mood disorders was always administered completely. When all criteria were met, BA started.

Baselines assessment in the lab (BA). Written and oral psychoeducation was provided (as requested by the target population in Vervaeke et al., 2018) about the study in general and more specifically regarding the training platform. The following questionnaires were administered: DASS, BDI-II, RRS, CERQ, QLDS, RDQ, CDRS, LTE, CEQ and ATQ-EC. Furthermore, participants completed a naPASAT as a baseline assessment of cognitive functioning. Lastly, information regarding the following phases, including instructions when encountering issues, was offered, again in a written and oral manner.

Online training phase. For each condition, the training procedure consisted of ten sessions of 15 minutes each. Participants were instructed to complete all sessions within a period of 14 days and to complete no more than one session per day. The training phase was administered online and started within two weeks following the BA. This forms a deviation from Hoorelbeke and Koster (2017), where the training was to be completed within a period of two weeks following the BA. After each session, participants were asked to schedule in the next session and automated reminders via e-mail were sent accordingly.

Cognitive control task. An aPASAT was used as a CCT task. Participants heard digits (ranging from 1 to 9) and had to continuously indicate the sum of the most recently heard pair of digits (i.e., after each digit). By adapting the intertrial interval, the difficulty of cognitive control training is adapted at an individual level. The intertrial interval decreased by 100 ms after four consecutive correct trials and increased by 100 ms after four consecutive incorrect or missed trials (as in Siegle et al., 2007; Hoorelbeke & Koster, 2017). In contrast to previous studies using the aPASAT training, the starting intertrial interval of each training session was based on the performance during the previous one. The ITI of the first session was based on performance on the naPASAT at baseline, offering a more individually tailored training approach.

Active control task. A speed-of-response training task was used as a low cognitive load variant of the aPASAT. Participants heard numbers (ranging from 1 to 18) and had to mark the corresponding response button with the same number on. The adaptive features of this task were identical to the CCT task. In addition, this task was visually identical to the CCT task and has repeatedly been used as an active control task (ACT) for CCT in previous studies (Hoorelbeke, Koster, Demeyer, Loeys, & Vanderhasselt, 2016; Hoorelbeke & Koster, 2017; Vervaeke, Hoorelbeke, Baeken, Van Looy, & Koster, 2019).

Online post-training assessment (PA). Participants were invited to complete an online post-training assessment within one week following completion of the final training session (as opposed to Hoorelbeke and Koster (2017), where this was the day following the last training session). The following questionnaires were administered: DASS, RRS, CERQ, QLDS, RDQ, CDRS, LTE, CEQ and UES. The naPASAT concluded this assessment.

Online follow-up assessment (FU 3M). Three months following completion of the last training session, participants were presented with another set of questionnaires and the naPASAT. Questionnaires in this set were DASS, RRS, CERQ, QLDS, RDQ, CDRS, and LTE.

Final follow-up assessment in the lab (FU 6M). As a last step in this study, participants were invited back to the lab, six months after the final training session. This assessment started with these questionnaires: DASS, BDI-II, RRS, CERQ, QLDS, RDQ, CDRS, LTE, and ATQ-EC. Again, the naPASAT followed. Lastly, participants received a written and oral debriefing. Participants were thanked and monetary compensation was provided.

Data Analysis

Analyses were conducted using SPSS Statistics 25. We used mixed ANOVAs to model effects of CCT on primary, secondary, and other outcome measures. Significance was set at $\alpha \leq .05$. All available data was included and all means and performance data on tasks and questionnaires are displayed in Table 3.

Due to a technical error in a part of the questionnaire assessment, there was data loss for about 40% of the participants at FU 6M, for the questionnaires RRS, LTE and ATQ-EC, and questions regarding current treatment. This data loss was not limited to one condition and affected 25 subjects in total (12 from the CCT group and 13 from the ACT group), resulting in complete data of 38 participants for FU 6M (Figure 1).

Table 3

Mean Scores on Questionnaires and Tasks, Divided by Group and Assessment, with Standard Deviations in Parentheses

	Cognitive control (N=34)				Active control (N=34)			
	BA	PA	FU 3M	FU 6M	BA	PA	FU 3M	FU 6M
naPASAT acc. (%)	34.2 (15)	73.2 (17)	68.5 (17)	65.2 (18)	29.4 (12)	39.7 (16)	38.3 (17)	40.0 (16)
DASS Depression	6.1 (5.3)	6.5 (7.9)	4.5 (4.8)	4.8 (5.4)	5.2 (6.2)	5.9 (7.9)	7.7 (8.5)	7.6 (7.6)
DASS Anxiety	4.0 (4.2)	3.7 (4.9)	3.4 (3.9)	3.4 (3.4)	4.3 (3.8)	3.5 (4.8)	5.0 (5.1)	5.2 (5.7)
DASS Stress	7.7 (6.1)	8.7 (6.9)	8.2 (8.3)	8.6 (6.6)	7.9 (5.9)	8.2 (6.6)	9.0 (6.4)	10.1 (7.0)
BDI-II	9.5 (6.8)	---	---	9.0 (5.7)	10.0 (7.3)	---	----	9.0 (6.5)
RRS	51.0 (10.6)	50.5 (10.3)	46.1 (12.0)	48.1 (12.8)	49.8 (12.7)	51.9 (12.2)	45.9 (12.5)	47.5 (11.4)
RRS Brooding	11.7 (3.4)	11.2 (3.2)	10.7 (3.2)	10.9 (3.5)	11.2 (3.5)	11.9 (3.5)	10.6 (3.7)	11.1 (3.5)
RRS Reflection	10.9 (2.6)	10.8 (3.0)	10.0 (2.8)	10.5 (3.1)	10.2 (3.3)	10.6 (3.3)	9.9 (3.3)	9.8 (3.4)
CERQ Adaptive	60.5 (15.4)	59.1 (14.8)	58.9 (15.2)	57.1 (17.4)	58.1 (12.3)	55.9 (12.5)	56.7 (12.2)	59.4 (16.1)
CERQ Maladaptive	36.7 (8.8)	35.3 (8.2)	33.4 (8.1)	34.3 (7.2)	37.4 (10.3)	37.7 (11.5)	35.5 (10.5)	35.8 (11.0)
QLDS	5.0 (5.6)	5.2 (6.4)	4.4 (6.5)	5.0 (5.6)	4.3 (5.4)	5.3 (6.4)	5.3 (6.5)	5.3 (5.7)
RDQ	23.6 (13.7)	22.1 (17.4)	19.4 (15.0)	23.7 (16.2)	22.1 (14.3)	22.1 (17.1)	24.7 (17.8)	26.1 (16.5)
CDRS	60.8 (14.1)	59.3 (14.5)	61.5 (13.2)	62.1 (14.4)	58.6 (14.3)	59.2 (13.6)	58.6 (14.2)	57.9 (14.8)
ATQ Effort. control	4.1 (1.0)	---	---	4.2 (1.0)	4.2 (0.8)	---	---	4.2 (0.8)
ATQ Activ. control	3.9 (1.1)	---	---	4.2 (1.3)	4.4 (1.1)	---	---	4.4 (1.0)
ATQ Attent. control	3.5 (1.3)	---	---	3.8 (1.4)	3.3 (1.0)	---	---	3.4 (0.8)
ATQ Inhib. control	4.6 (1.2)	---	---	4.6 (1.1)	4.5 (1.0)	---	---	4.6 (1.0)
UES	---	94.0 (16.0)	---	---	---	93.4 (18.4)	---	---
CEQ Credibility	0.1 (2.3)	0.2 (2.2)	---	---	-0.1 (2.2)	-0.2 (2.7)	---	---
CEQ Expectancy	-0.1 (2.4)	0.3 (2.8)	---	---	0.02 (2.6)	-0.03 (2.8)	---	---
LTE	1.6 (1.4)	0.4 (0.6)	0.5 (0.7)	1.0 (1.0)	1.3 (1.4)	0.2 (0.4)	0.4 (0.6)	0.7 (0.9)

naPASAT = non-adaptive Paced Auditory Serial Addition Task; DASS = Depression Anxiety Stress Scales; BDI-II = Beck Depressive Inventory II; RRS = Ruminative Response Scale; CERQ = Cognitive Emotion Regulation Questionnaire; QLDS = Quality of Life in Depression Scale; RDQ = Remission from Depression Questionnaire; CDRS = Connor-Davidson Resilience Scale; ATQ Effort. control = Effortful control; ATQ Activ. control = Activation Control; ATQ Attent.control. = Attentional Control; ATQ Inhib. control = Inhibitory Control (previous four abbreviations from the Adult Temperament Questionnaire); UES = User Engagement Scale; CEQ = Credibility/Expectancy Questionnaire; LTE = List of Threatening Experiences

Missing data were handled with the Last Observation Carried Forward method and Intention-To-Treat analyses were conducted. In addition, as secondary analyses, we engaged in Completers-Only analyses and this is then reported as such.

Results

Sample Characteristics

Sample characteristics are displayed in Table 1. There were no pre-existing differences between the two groups for most variables. However, they did differ significantly in terms of age and number of depressive episodes. When adding these two variables (age and number of depressive episodes) as covariates in the analyses, results did not change drastically[2]. The analyses reported below do not include these covariates. Furthermore, there were no differences in duration between groups, in terms of training phase or days between assessments (Table 1).

Training Progression

Progress during training was analyzed separately for the two training conditions (as in Hoorelbeke et al., 2016; Hoorelbeke & Koster, 2017; Vervaeke et al., 2019). Two repeated measures ANOVAs showed that, as expected, median intertrial intervals decreased, meaning that participants improved significantly, on both training tasks: $F(2.7, 88.2) = 73.62$; $p < 0.001$; $\eta_p^2 = 0.69$ for the CCT group and $F(1.9, 61.7) = 9.88$; $p < 0.001$; $\eta_p^2 = 0.23$ for the ACT group. The median intertrial intervals are displayed in Figure 2.

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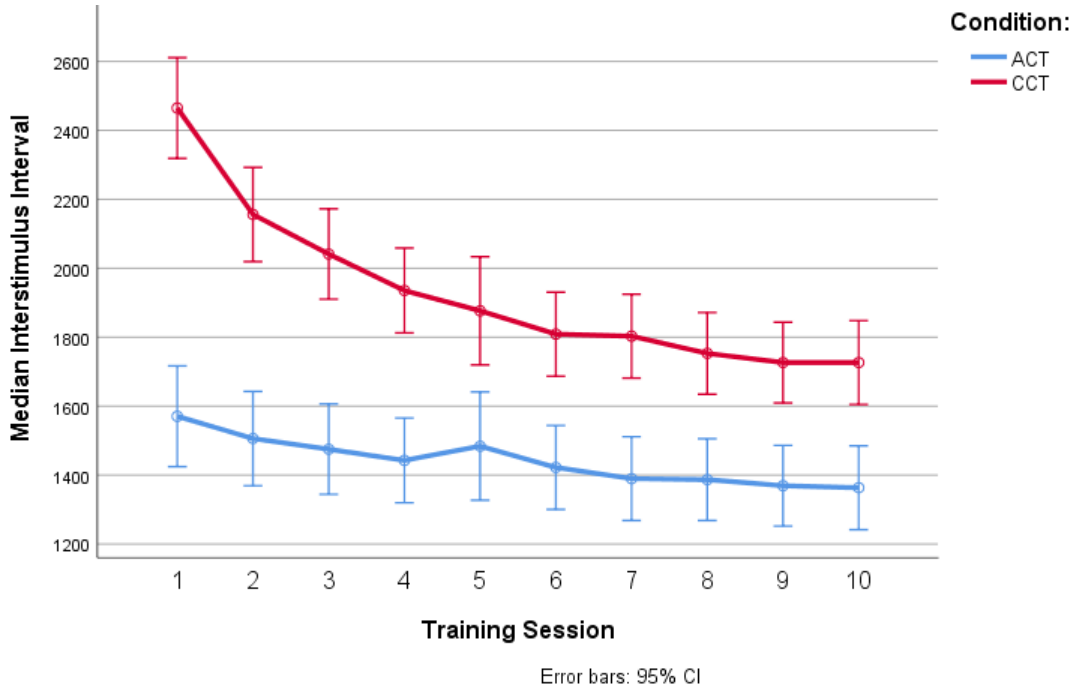
[2] However, there was an interesting impact of these covariates when analyzing scores on the RDQ. This will be further illustrated in the corresponding paragraph.

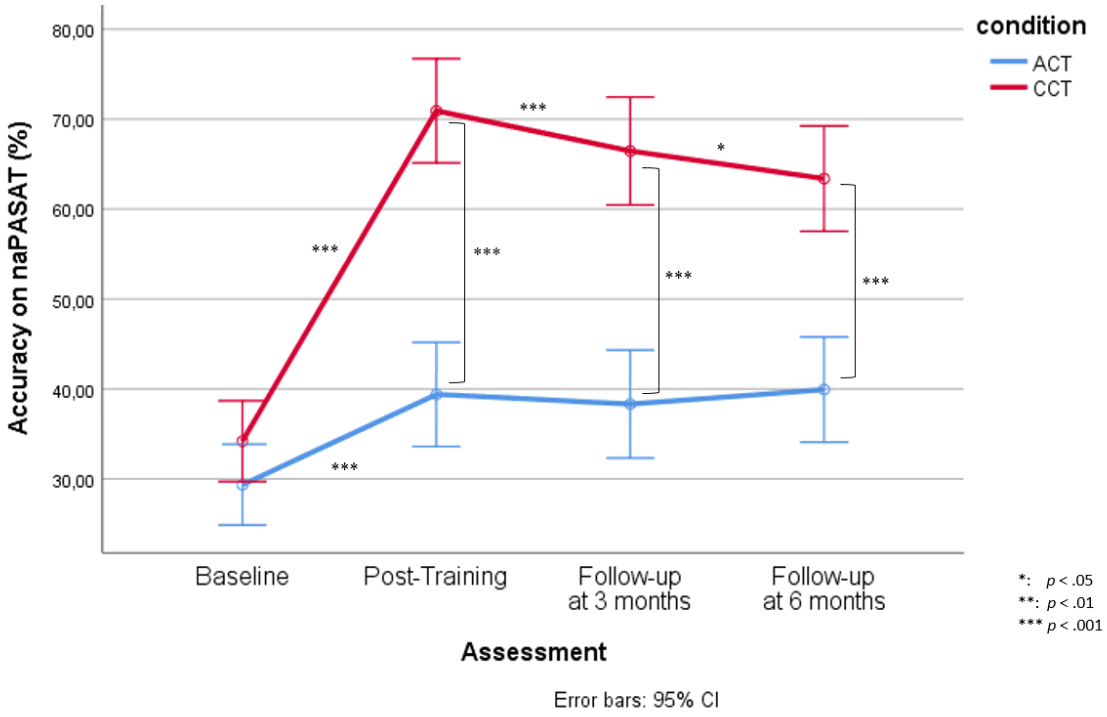
Figure 2. Progress over Training Sessions for the Two Training Conditions.



Task-Specific Cognitive Transfer

Cognitive transfer effects were assessed using a 4 (time: BA, PA, FU 3M, FU 6M) by 2 (training: CCT, ACT) Mixed ANOVA on naPASAT accuracy. There was a significant transfer effect, indicated by a significant time x training interaction: $F(1.8, 121.9) = 43.27$; $p < 0.001$; $\eta_p^2 = 0.40$. Independent samples *t*-tests suggest a significant difference between groups in terms of cognitive task performance at PA, FU 3M and FU 6M. Thus, even after six months without training, task-specific cognitive transfer remained present. In addition, using paired samples *t*-tests, we observed an increase in task performance from BA to PA in the CCT condition. From PA to FU 3M, and from FU 3M to FU 6M, task performance slightly declined again. Similarly, participants in the ACT condition showed an increase from BA to PA. However, scores did not decrease but remained stable in this group. Scores and significance of follow-up *t*-tests are shown in Figure 3.

Figure 3. Task-Specific Cognitive Transfer over Time, for Both Conditions.



Primary Outcome Measures

In terms of *depressive symptomatology*, there was no main effect of time or training task on any of the DASS subscales. Importantly, there was a significant interaction of time by training for the depression subscale (Table 4). Follow-up independent samples *t*-tests showed no difference between groups at PA ($t(66) = 0.31$; $p = .760$; $d = 0.07$), yet there was a marginally significant difference at FU 3M ($t(51.9) = 1.89$; $p = .064$; $d = 0.46$) and FU 6M ($t(59.9) = 1.74$; $p = .088$; $d = 0.42$), where the CCT group reported a trend for less depressive symptomatology than the ACT group. No interaction effects were found for the stress and anxiety scale of the DASS.

These effects were not corroborated on any of the other primary outcome measures. Modeling effects of CCT on the BDI-II, which was only assessed at BA and FU 6M, we did not find an effect of training task, time nor an interaction (Table 4). Similar results were obtained using Completers-Only analysis.

Table 4

Test Statistics for Training Effects from Mixed ANOVAs

	Main effect of time				Main effect of training task				Time x task interaction			
	F	*df*	*p*	η_p^2	*F*	*df*	*p*	η_p^2	*F*	*df*	*p*	η_p^2
naPASAT	141.3	1.8, 121.9	<.001	0.68	36.9	1, 66	<.001	0.36	43.3	1.8, 121.9	<.001	0.40
DASS D	0.2	2.7, 177.4	.878	<0.01	0.7	1, 66	.404	0.01	3.4	2.7, 177.4	.022	0.05
DASS A	0.6	3, 198	.585	0.01	1.0	1, 66	.311	0.02	1.6	3, 198	.183	0.02
DASS S	1.2	3, 198	.309	0.02	0.2	1, 66	.694	<0.01	0.5	3, 198	.665	0.01
BDI-II	1.2	1, 66	.286	0.02	0.03	1, 66	.865	<0.01	0.1	1, 66	.727	<0.01
RRS	10.5	3, 198	<.001	0.14	0.01	1, 66	.946	<0.01	0.6	3, 198	.604	0.01
RRS B	3.5	3, 198	.017	0.05	0.01	1, 66	.906	<0.01	1.2	3, 198	.295	0.02
RRS R	2.8	2.7, 175.8	.049	0.04	0.3	1, 66	.578	0.01	0.5	2.7, 175.8	.695	0.01
CERQ Ad	0.7	3, 198	.554	0.01	0.2	1, 66	.657	<0.01	1.8	3, 198	.152	0.03
CERQ M	3.4	3, 198	.018	0.05	0.7	1, 66	.408	0.01	0.3	3, 198	.804	0.01
QLDS	0.4	2.7, 180.1	.741	0.01	0.01	1, 66	.919	<0.01	0.5	2.7, 180.1	.644	0.01
RDQ	1.1	3, 198	.372	0.02	0.2	1, 66	.639	<0.01	1.3	3, 198	.274	0.02
CDRS	0.2	2.7, 177.6	.892	<0.01	0.6	1, 66	.459	0.01	1.2	2.7, 177.6	.323	0.02
Effortf. C.	6.4	1, 66	.014	0.09	0.04	1, 66	.834	<0.01	1.7	1, 66	.201	0.03
Act. C.	4.5	1, 66	.037	0.06	1.1	1, 66	.288	0.02	6.7	1, 66	.012	0.09
Att. C.	7.6	1, 66	.007	0.10	0.9	1, 66	.344	0.01	1.9	1, 66	.177	0.03
Inh. C.	0.7	1, 66	.391	0.01	<0.1	1, 66	.985	<0.01	1.4	1, 66	.236	0.02
CEQ C	<0.01	1, 66	.993	<0.01	0.4	1, 66	.512	0.01	0.1	1, 66	.812	<0.01
CEQ E	0.4	1, 66	.532	0.01	0.1	1, 66	.817	<0.01	0.6	1, 66	.424	0.01
LTE	13.6	2.1, 71.8	<.001	0.28	0.9	1, 35	.352	0.03	0.2	2.1, 71.8	.810	0.01

naPASAT = non-adaptive Paced Auditory Serial Addition Task; DASS = Depression Anxiety Stress Scales; D = Depression; A = Anxiety; S = Stress; BDI-II = Beck Depressive Inventory II; RRS = Ruminative Response Scale; B = Brooding; R = Reflection; CERQ = Cognitive Emotion Regulation Questionnaire; Ad = Adaptive; M = Maladaptive; QLDS = Quality of Life in Depression Scale; RDQ = Remission from Depression Questionnaire; CDRS = Connor-Davidson Resilience Scale; Effortf. C. = Effortful Control; Act. C. = Activation Control; Att. C. = Attentional Control; Inh. C. = Inhibitory Control (previous four abbreviations from the Adult Temperament Questionnaire); CEQ = Credibility/Expectancy Questionnaire; LTE = List of Threatening Experience

In addition, *depressive rumination* decreased for both groups, as reported by a significant time effect on the total score of the RRS, and on the brooding and reflection subscale. However, there were no effects of training or significant interactions on the full scale or on either subscale (Table 4). This pattern of results was replicated with Completers-Only analyses.

Secondary Outcome Measures

Except for a main effect of time for maladaptive emotion regulations, no significant main or interaction effects were observed for use of *(mal)adaptive emotion regulation strategies* (CERQ; Table 4). *Quality of life* scores (QLDS) were not impacted by time or training task and there was no significant interaction (Table 4). *Residual symptoms*, as reflected by the RDQ, did not show an effect of time, training task, nor an interaction (Table 4). In contrast to the other analyses, the outcome of this analysis was affected by the baseline differences in age and number of depressive episodes. That is, when adding age and number of depressive episodes as covariates in this analysis, the interaction became marginally significant ($F(3, 192) = 2.4$; $p = .070$; $\eta_p^2 = 0.36$) and a trend for a reduction of residual complaints from PA to FU 3M was observed for the CCT group, compared to an increase in the ACT condition. Visually, scores seemed different between conditions at 3M FU but this effect has disappeared at FU 6M. Given that Hoorelbeke and Koster (2017) analyzed residual symptomatology only at BA and at FU 3M, we conducted their exact analysis (2x2 Mixed ANOVA) as well in a post hoc fashion, which showed a marginal significant interaction ($F(1, 66) = 3.28$; $p = .075$; $\eta_p^2 = 0.05$). When controlling for age and number of depressive episodes, this interaction became significant ($F(1, 64) = 6.55$; $p = .013$; $\eta_p^2 = 0.09$). Neither time or training task affected the *resilience* scores (CDRS) and no interaction was found (Table 4). Performing completers-only analyses did not affect results regarding these secondary outcome measures.

Other Outcome Measures

Related to cognitive control, *effortful control* improved in both groups. Looking into each component of effortful control separately, activation and attentional control showed an increase over time, but inhibitory control did not. Additionally, a time by training interaction was found for the subscale activation control (Table 4). However, follow-up independent *t*-tests failed to show group differences at FU 6M (all *t*s < 1.28; all *d*s < 0.31). Follow-up paired samples *t*-tests suggested no change over time in activation, attentional, and inhibition control within the ACT group, meaning a stable score across time points for this group was observed (all *t*s < 1.43; all *d*s < 0.25). The CCT group on the other hand showed an increase in overall effortful control ($t(33) = 2.30$; $p = .028$; $d = 0.39$), attentional control ($t(33) = 2.64$; $p = .013$; $d = 0.45$) and activation control ($t(33) = 2.77$; $p = .009$; $d = 0.48$), but not on inhibitory control ($t(33) = 0.24$; $p = .811$; $d = 0.04$).

Control Measures

User engagement was assessed only once, making an intention-to-treat analysis impossible. The completers-only analysis included data from 65 participants and consisted of a two-sided independent samples *t*-test. This showed no difference between the two groups, meaning that the two training tasks were rated equally engaging ($t(63) = 0.16$; $p = .877$; $d = 0.04$), allowing to control for motivational effects on training.

Credibility and expectancy scores did not differ across the two groups, or across time points. Thus, there did not seem to be motivational differences between the two training conditions (Table 4).

As important negative events can impact questionnaires scores, we assessed these as well. In the LTE, data cannot be handled with the Last Observation Carried Forward method. Therefore, we conducted a Mixed ANOVA on 37 participants who had complete data, which

showed no differences between groups. Furthermore, independent samples *t*-tests revealed no differences between the two training groups, at all assessments, when including all available data (which was $N = 68$; $N = 65$; $N = 62$; $N = 38$ for BA, PA, FU 3M and FU 6M, respectively).

Discussion

In the current study, we aimed to replicate and extend the findings of Hoorelbeke and Koster (2017) using our new cognitive control training (CCT) platform. We randomly assigned remitted depressed individuals to either the CCT or an active control condition. Assessments were conducted at baseline, immediately following training, and three and six months after training. The current study provides a partial replication of the previously observed effects (Hoorelbeke & Koster, 2017). That is, we observed stable task-specific cognitive transfer and a decrease in some but not all indicators of depressive symptomatology. We will discuss these findings in more detail below.

Importantly, we observed task-specific cognitive transfer. That is, participants in the CCT condition showed improved performance on a cognitive task. Moreover, we also observed beneficial effects of training on self-reported effortful control, an indicator of cognitive functioning. In particular, scores increased for attentional and activation control but only in the CCT group, and there was an interaction effect for activation control. These findings are important provided that depression has been linked to lower scores on this effortful control scale. For instance, Kanske and Kotz (2012) showed opposite correlational patterns for depression and effortful control in a range of experiments on conflict processing. While higher depression scores were correlated with slower conflict processing, higher effortful control was associated with faster conflict processing. However, they did not investigate the correlation between depression and effortful control directly. Furthermore, Moriya & Tanno (2008) found a negative association between the activation control component and depression, as measured by Zung's Self-rating Depression Scale (1965) which has a strong correlation with the DASS Depression scale (Pearson's r = .78; Dunstan, Scott, & Todd, 2017). These findings are in line with our data, where we observed a decrease in depressive symptomatology and an increase in activation control in the CCT group.

However, the time by condition interaction on activation control needs to be interpreted with caution. The increase in activation control scores for the CCT group might reflect a regression to the mean. Interestingly, using an alternative indicator of cognitive functioning (self-reported working memory complaints), Hoorelbeke and Koster (2017) observed a marginally significant effect of CCT (completers-only). There, the CCT group seemed to improve while the scores of the ACT group remained stable. This pattern of results resembles our findings with the ATQ-EC, although our time frame was extended.

The findings regarding residual symptomatology also warrant discussion. An interaction effect between time and training emerged on the RDQ that was marginally significant. This interaction was present only when adding the covariates age and number of depressive episodes, which differed between conditions at baseline. In this interaction, residual symptomatology seemed to decrease in the CCT group and increase in the ACT group, from PA to FU 3M. However, follow-up *t*-tests (without covariates) failed to show group differences and these trend for effects disappeared again at FU 6M. As the RDQ in Hoorelbeke and Koster (2017) was only measured at BA and FU 3M, we analyzed data post-hoc in this manner. This yielded a marginal interaction, and this interaction reached significance when controlling for age and number of depressive episodes, replicating the original effect found by Hoorelbeke and Koster (2017). It is possible that the CCT led to a small and temporary decrease in residual symptomatology. Although this finding suggests that previously observed effects of CCT on the RDQ are replicable (3M FU), the effects are small and need to be interpreted cautiously. In particular, the effect seems to be limited in time, suggesting no lasting beneficial effects six months following training.

Additionally, some effects were not replicated. First, we did not find any effects on depressive symptomatology as measured with the BDI-II. We believe that this might be due to the fact that the BDI-II was only re-assessed at FU 6M. Fluctuation of scores in-between

these time points could be obscured if these effects are temporary and thus, no longer observable at final assessment. In line with this claim, the DASS Depression scale shows smaller effects at FU 6M than at FU 3M. Similarly, effects of CCT on the RDQ did not last until FU 6M. Second, the RRS and its subscales did not show any effects apart from a decrease over time, for both conditions. The original study of Hoorelbeke and Koster (2017) reported decreasing scores over time for both groups, but this decrease was greater for the CCT group, which we could not replicate. Noted, given that we lacked a substantial amount of data on this measure, our power was substantially decreased due to data loss, increasing difficulty of finding effects. Third, we were unable to replicate findings on some secondary outcome measures as well. Hoorelbeke and Koster (2017) found clear effects on maladaptive emotion regulation strategies and resilience, but we did not. Moreover, we could not find any effects regarding quality of life, while the original study showed some mixed evidence here. Lastly, we replicated the null findings regarding adaptive emotion regulation strategies.

Even though the method was highly similar, we were only able to replicate some of the previously observed beneficial effects of CCT. The reason for this is unclear. In the following part, we aim to describe the most prominent differences between studies. A first difference was our selected sample as we applied less strict inclusion criteria. It sufficed when participants were in remission for at least three months (instead of six months). Furthermore, we also included participants that had suffered from bipolar depression (instead of only unipolar). At BA, eight participants were in remission for a period between three and six months and all eight, through randomization, were assigned to the ACT group. However, there were no baseline differences between this subset of eight participants, and the remainder of the sample, except for anxiety scores that were higher in the rest of the sample. Furthermore, ten participants had suffered from at least one (hypo)manic episode in the past, with six of them being assigned to the CCT group. Of these ten, two participants did not

complete training, one in each condition. Checking for baseline differences showed a difference on the ATQ-EC, with the unipolar group having higher scores for overall effortful control and inhibitory control. Furthermore, at FU 6M, these differences remained, with higher scores for the unipolar group in terms of overall effortful control, attentional control and inhibitory control as shown with independent *t*-tests. As the interaction between type of depression and time was not significant, we believe the uni- and bipolar groups had similar effects from training, even though this analysis might be underpowered. In addition, there was a difference between conditions at baseline for age and number of depressive episodes, which both are predictors for relapse. Controlling for these differences did not impact results (except for findings regarding the RDQ). Overall, although we used broader criteria, the samples were similar.

A second difference was the response button layout and surrounding software. This layout was based on input from remitted depressed individuals during development (Vervaeke et al., 2018), that disliked the original task layout used by Hoorelbeke and Koster (2017). Therefore, we changed this to a layout that diminished the distance between response buttons. However, we do not believe that this has an impact, given that previous studies, such as Siegle et al. (2007; 2014) use yet another response button pattern (in a diamond shape). Furthermore, the task was still identical, even though certain parameters might be deviating slightly, so participants should have recruited the same brain regions and this should have had a comparable effect.

A third difference related to dosage of training. While every training session in Hoorelbeke and Koster (2017) consisted of 400 trials, we implemented a fixed training duration of 15 minutes, resulting in a varying number of trials per person and per session. Given that limited training fails to impact cognitive functioning (Koster et al., 2017), this is an important issue. Even though we found a strong cognitive transfer effect and progress

during training, we examined the number of trials in our training to ensure adequate training dosage. There were seven participants in the CCT group with less than 400 trials on average. For all but one, at least one session contained more than 400 trials. All other participants had on average over 400 trials per session. Therefore, we state that our training dosage was in line with Hoorelbeke and Koster (2017). However, what amount of training dosage is adequate in this context remains an important research question.

In short, even though there were some deviations in methodology from the original study, we believe none of them can explain the difference in findings between the original and the replication study. Moreover, there was a lot of variability in our data with relation to clinical outcomes and cognitive functioning. An interesting avenue for further research would be to investigate moderators of effectiveness of CCT, which might explain the differences found between our study and the one we tried to replicate, and other CCT studies. By confirming already observed moderators and identifying new moderator variables, effects of CCT might become clearer and insights on underlying mechanisms can be gained, ensuring more consistent results and precisely targeted implementation of this training as a preventive intervention for certain subgroups of (remitted) depressed individuals.

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Chapter 6: Examining Moderators of Cognitive Control Training: An Effectiveness Trial in High Worriers

Abstract

In recent years, there have been several training studies aimed at improving cognitive control in order to decrease vulnerability for depression. Although overall beneficial effects have been reported, individual studies demonstrate mixed results. The aim of this study is to identify moderator variables that affect effectiveness of cognitive control training in the context of depression.

The current study was registered on the Open Science Framework (osf.io/8ymd9) and consisted of administering online cognitive control training to a large and varied sample of self-identified worriers. Assessments took place before and after training, and one month later. Demographic variables, personality, general functioning, effortful control, cognitive control, repetitive negative thinking, symptomatology, resilience and engagement were included as potential moderators of effectiveness.

In total, 311 participants started baseline assessment, 157 completed all training sessions and 125 participants completed the full study protocol. Even though there was no control condition present, training effects in this study are large and comparable to other cognitive control training studies. Specifically, improvements were found on nearly all measurements. Age predicted outcomes consistently, with older participants benefitting less from training. This effect was more pronounced when cognitive control was low at baseline. Highly engaged and less resilient participants showed greater improvements.

Introduction

Vulnerability for Depression

Major depressive disorder is a common and severe mood disorder (Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012). There are several evidence-based treatments available that show positive outcomes in terms of short-term effects (Cuijpers, 2017). However, relapse and recurrence rates are problematic, and most depressed patients will encounter multiple depressive episodes (Kessler et al., 2012). For instance, a longitudinal study showed that in a sample of remitted patients, 79% had at least one recurrence within 5.5 years, (Bockting, Spinhoven, Wouters, Koeter, & Schene, 2009), demonstrating that these treatments possibly fail in altering underlying vulnerability mechanisms.

One of these proposed vulnerability mechanisms is impaired cognitive control. Indeed, cognitive control deficits have been observed during depressive episodes (Snyder, 2013; Rock, Roiser, Riedel, & Blackwell, 2014; Gotlib & Joormann, 2010; Baune, Miller, McAfoose, Johnson, Quirk, & Mitchell, 2010), frequently remain present during remission when depressive complaints have subsided (Semkovska et al., 2019; Rock et al., 2014), and can even predict new episodes (Majer et al., 2004).

Cognitive control is a collection of processes, such as updating, monitoring and inhibiting information in working memory, responsible for adapting thoughts and behaviors in line with current goals, in a flexible manner (Botvinick & Braver, 2015; Miyake et al., 2000). Impaired cognitive control can be reflected in several cognitive biases, such as attentional, memory and interpretation bias, since these impairments affect information processing. For instance, depressed individuals sometimes show an elevated tendency to direct attention at negative vs. neutral stimuli, compared to healthy individuals. Some theories have argued for a general cognitive control impairment in depression (Snyder, 2013) while

others claim that there is an emotion-specific impairment leading to biases in the processing of negative stimuli (Joorman, Levens, & Gotlib, 2011; Joormann & Gotlib, 2008). Although debate is still ongoing, a link between cognitive control and emotion regulation has been demonstrated (e.g., Zetsche, Bürkner, & Schulze, 2018). Deficient emotion regulation, and rumination in particular, is a well-established vulnerability factor for maintenance and recurrence of depressive episodes (for a review, see Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008).

Rumination is a passive and repetitive thinking style that focuses attention on symptoms, and causes and consequences thereof, rather than on solutions (Nolen-Hoeksema, 1991), which has a clear connection with depression (Olatunji, Naragon-Gainey, & Wolitzky-Taylor, 2013; Nolen-Hoeksema et al., 2008) and can predict future depressive episodes (Kuehner & Weber, 1999; Spasojevic & Alloy, 2001). Furthermore, impairments in cognitive control can contribute to difficulties with controlling negative thoughts and rumination (Joormann & D'Avanzato, 2010; Zetsche & Joormann, 2011). Repetitive negative thoughts are considered transdiagnostic processes that can be observed in depression as well as many other mental disorders.

Repetitive negative thinking (RNT) is a thinking style characterized by repetitive, negative, and uncontrollable thoughts, that are experienced as intrusive and difficult to disengage from (Ehring & Watkins, 2008). At least 13 psychological disorders, including mood and anxiety disorders, insomnia, post-traumatic stress disorder, and psychosis, show elevated levels of this style of thinking. Moreover, it is regarded as a transdiagnostic maintenance and risk factor for multiple mental disorders (McEvoy, Watson, Watkins, & Nathan, 2013; McLaughlin & Nolen-Hoeksema, 2011; Watkins, 2008; Sloan, Hall, Moulding, Bryce, Mildred, & Staiger, 2017). Indeed, no differences were found between patients with major depressive disorder, generalized anxiety disorder, and obsessive-

compulsive disorder, in terms of content-independent characteristics of RNT, while this was increased compared to healthy controls (Wahl et al., 2019). Thus, rumination can be assumed to be a form of RNT applied in the context of depression. Future depressive symptomatology has been predicted by RNT (Ehring, Frank, & Ehlers, 2008). It was predictive for other disorders as well, including anxiety (Siddique, LaSalle-Ricci, Glass, Arnkoff, & Diaz, 2006), post-traumatic stress disorder (Ehring et al, 2008), and bulimia and alcohol abuse (Nolen-Hoeksema et al., 2007).

Cognitive Control Training

Cognitive control impairments are considered a risk factor for the development of depression, through their association with emotion regulation. That is, impaired cognitive control and depression can result in a reduced ability to control RNT. Provided the importance of emotion regulation, it has been argued that improving cognitive control can have beneficial effects. Cognitive control training (CCT) is being investigated increasingly as a means to remediate these risk factors. Individual studies pertaining CCT show beneficial effects on cognitive functioning, depressive symptomatology and rumination. However, some studies failed to find such effects (for an overview, see Koster, Hoorelbeke, Onraedt, Owens, & Derakshan, 2017).

Given these mixed findings, research into moderators for effectiveness of CCT is pertinent. So far, this research is limited. Only two studies have looked into this, as secondary research questions. Brunoni et al. (2014) administered CCT to depressed patients, in combination with real vs. sham neurostimulation aimed at hypoactive brain regions during depression. Results showed a decrease for both groups in terms of depressive symptomatology, which was more pronounced in younger patients, showing a potential influence of age. Additionally, limited evidence was found for an impact of training task

improvement. Gender, length of depressive episodes, age of onset, number of episodes, medication use and baseline cognitive control functioning showed no impact on effectiveness, but finding differential effects between conditions was the primary aim, rather than identifying moderators of CCT effectiveness, and sample size was limited (N = 37).

In a second study, CCT compared to treatment as usual in a depressed sample resulted in decreased rumination and diminished need for patient services. Furthermore, data suggested that task engagement before intervention, as measured with pupil dilation, strengthened these effects (Siegle, Price, Jones, Ghinassi, Painter, & Thase, 2014).

Current study: Searching for Moderating Variables

In this study, we will administer CCT to a large group of individuals with different backgrounds to increase variability. Our aim is to identify variables that moderate effects of CCT. Therefore, a wide array of potential moderating variables was included (demographic variables, personality traits, emotion regulation, functioning, cognitive control and engagement) as displayed in Table 1. We differentiate between stable variables (hereafter referred to as *trait variables*) that will be measured once, and mental health variables that are thought to vary over time (referred to as *state variables*) and will be assessed several times.

Table 1

Variables Included in this Study

Possible moderators	Justification
Trait	
Demographics	Age might be a moderator (Brunoni et al., 2004)
Personality	Neuroticism is associated with anxiety and depression (Muris, Roelofs, Rassin, Franken, & Mayer, 2005)
	Personality traits show a clear link with rumination (Barańczuk, 2019) and emotion regulation (Wang, Shi, & Li, 2009)
Effortful control	Effortful control can be regarded as an indicator of cognitive control on a trait level (Nigg, 2017)
Overall functioning	This is affected by cognitive impairment (Baune et al., 2010)
Engagement	Task engagement might be a moderator (Siegle et al., 2014)
State	
RNT	This is an important risk factor for a range of psychopathology (Ehring & Watkins, 2008; Ehring et al., 2008)
Symptomology	Having subclinical symptoms is a risk factor for for instance depression (Horwath, Johnson, Klerman, & Weissman, 1992)
Emotion regulation	Several strategies are associated with depression (Aldao, Nolen-Hoeksema, & Schweizer, 2009), in particular
	suppression and reappraisal (Ehring, Tuschen-Caffier, Schnülle, Fischer, & Gross, 2010)
Resilience	Resilience predicts several vulnerability factors (Hoorelbeke, Van den Bergh, Wichers, & Koster, 2019)

Method

Design

This study was approved by the medical ethical committee and preregistered on the Open Science Framework (osf.io/8ymd9). This study was conducted fully online and the protocol consisted of the following steps: (1) baseline assessment, (2) cognitive control training (CCT), (3) post-training assessment, and (4) follow-up assessment. All phases were identical for all participants as all participants were allocated to the CCT condition. After completion of baseline assessment, participants were requested to start the training phase within two weeks and to complete the post-training assessment within one week after the last training session. The follow-up assessment was scheduled one month after completion of the final training session.

Sample

The sample consisted of Dutch-speaking adults between 18 and 70 years of age that were recruited via traditional and social media. This study was framed as a new, online and freely accessible intervention to reduce RNT. In other words, our sample consisted of self-identified repetitive negative thinkers although we did not screen for this explicitly. People that were suffering from severe depressive complaints were discouraged to participate. Participants needed to be able to use a computer or tablet regularly, with internet access. Electronic informed consent was obtained for all participants. Two €50 shopping vouchers were raffled for participants that completed the full protocol. No individual monetary incentives were provided.

Cognitive Control Training

All participants received the same intervention: cognitive control training, consisting of ten sessions of adaptive Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977; Siegle, Ghinassi, & Thase, 2007), in a gamified context. Participants were instructed to complete all ten sessions over a period of two weeks and advised to do no more than one session daily. Every session lasted for 15 minutes. In this task, participants heard single digits (1-9) in a random order, and needed to indicate the sum of every last heard digit with the one presented just before in a continuous manner. Thus, after every digit a response was due. As this was an adaptive training task, difficulty was set at an individualized level. Based on performance, the intertrial interval increased or decreased (as in Siegle et al., 2007; Hoorelbeke & Koster, 2017; Vervaeke, Hoorelbeke, Baeken, Van Looy, & Koster, 2019). Specifically, after four correct responses the presentation speed of the digits increased with 100 ms. After four incorrect, late or missing responses, this speed decreased with 100 ms. The beginning intertrial interval of every session was based on performance in the session before. For the first session, this was based on performance during baseline assessment (see later). Previous research showed that gamifying this task (i.e., adding game elements such as points and levels) was associated with increased user engagement and motivation without altering training mechanisms (Vervaeke et al., 2019). Therefore, we chose this gamified training version for the current study, in order to promote a positive user experience and maximize engagement, which might result in fortified effects (Siegle et al., 2014). In particular, this meant a vivid and colorful look, additional performance feedback, motivating messages during the task, auditory cues and a badge system for completing sessions (for a full overview, see Vervaeke et al., 2019).

Potential Moderators

A range of potential moderators was examined in this study. On the one hand, some variables were considered to be traits or stable and were measured only once. On the other hand, state variables were assessed on multiple occasions. All questionnaires were in Dutch.

Trait variables. *Demographic information* was collected. Specifically, information regarding age, gender, education level, employment status, math affinity and fear, and medication for mental health was obtained. Furthermore, *personality traits* were examined using the Ten Item Personality Inventory (TIPI; Gosling, Rentfrow, & Swann, 2003; Hofmans, Kuppens, & Allik, 2008). Each of the ten items measures one pole of the five bipolar personality dimensions of the Big Five personality framework and this scale results in a score for each of the five dimensions (extraversion, agreeableness, conscientiousness, emotional stability, and openness to experience). *Overall functioning* was measured with the Remission from Depression Questionnaire (RDQ; Zimmerman et al., 2013; Peeters, Nicolson, Wichers, & Hacker, 2013), but wording was slightly altered as the sample was not necessarily remitted from depression. Nevertheless, this questionnaire was used because it forms a broad yet inclusive measure of functioning in several domains: depressive symptoms, other symptoms, coping, positive mental health, general functioning, life satisfaction, and sense of well-being. The subscale Effortful Control of the Adult Temperament Questionnaire was administered as well (EC; Rothbart, Ahadi, & Evans, 2000; Hartman & Rothbart, 2001) and is a measure of *cognitive functioning*. It contains 19 items constituting three components (attentional control, activation control, and inhibitory control). Lastly, *user engagement* was collected with the short form of the User Engagement Scale (UES; O'Brien, Cairns, & Hall, 2018). These twelve items belong to four components (focused attention, perceived usability, aesthetic appeal, reward).

State measures. *Cognitive control* was measured behaviorally, using a non-adaptive PASAT version (naPASAT; Gronwall, 1977; Siegle et al., 2007). As in the adaptive versions, participants hear digits between 1 and 9, and after every digit, need to indicate the sum of the last two digits. However, this task consists of 180 trials, divided over three blocks with increasing intertrial interval and thus difficulty (but these intervals were fixed within blocks: Block 1, 3000 ms; Block 2, 2000 ms; Block 3, 1500 ms). The outcome of interest is mean accuracy over the three blocks. As opposed to the adaptive training task, difficulty is the same for all participants, measuring cognitive control in a standardized manner.

The Perseverative Thinking Questionnaire (PTQ; Ehring, Zetsche, Weidacker, Wahl, Schoenfeld, & Ehlers, 2011; Ehring, Raes, Weidacker, & Emmelkamp, 2012) was used to examine *repetitive negative thinking (RNT).* This 15-item questionnaire contains three components relating to the characteristics of RNT: core properties (repetition, intrusion, and uncontrollability), unproductiveness and use of mental capacity. *Symptomatology* was investigated using the 21-item version of the Depression Anxiety Stress Scales (DASS; Lovibond & Lovibond, 1995; de Beurs, Van Dyck, Marquenie, Lange, & Blonk, 2001). The three subscales measure depressive, anxiety, and stress symptoms. The use of *emotion regulation strategies* was assessed with the ten items from the Emotion Regulation Questionnaire (ERQ; Gross & John, 2003). The ERQ measures an adaptive and a maladaptive emotion regulation strategy, namely reappraisal and suppression. Lastly, r*esilience* was measured by the 10-item version of the Connor-Davidson Resilience Scale (CDRS; Connor & Davidson, 2003; translated by Danhof-Pont and Schrier).

Procedure

Recruitment phase. Potential participants were able to express their interest in participation by contacting us, upon which they received all information including psychoeducation. After explicitly agreeing to participate in a follow-up e-mail, they received practical information to begin the study. Visiting the training platform for the first time, participants were prompted with an electronic informed consent.

Baseline assessment. The first step in the baseline assessment consisted of a summary of psychoeducation regarding this study with some multiple choice questions, to ensure participants read all necessary information. Afterwards, participants received the following questionnaires: demographic information, PTQ, RDQ, ERQ, TIPI, DASS, CDRS, and EC. Upon completion, they were administered the naPASAT, which was preceded with a video tutorial and a practice phase. Baseline assessment was estimated to last between 30 and 40 minutes.

Training phase. Participants were asked to start training within two weeks following baseline assessment. Training consisted of ten sessions and participants were instructed to complete all ten sessions over a period over 14 days, with no more than one session per day. Each session consisted of 15 minutes of aPASAT. At the end of every session, participants were asked to schedule the next training session and automated reminder e-mails were sent accordingly.

Post-training assessment. Upon completion of the training - or when participants stopped performing training sessions - a second assessment was administered. Instructions asked that participants completed this assessment between 1 and 7 days following the last training session. This assessment contained the following questionnaires: UES, PTQ, ERQ,

DASS, and CDRS. The naPASAT was also administered in an identical manner as during baseline assessment. This assessment had a length of 15 to 20 minutes.

Follow-up assessment. Participants received an e-mail invitation to complete the final assessment, one month following the last training session. This assessment included these questionnaires: PTQ, ERQ, DASS, and CDRS. Furthermore, the naPASAT was administered for the third and final time. Assessment duration was 15 to 20 minutes.

Dropout. In case participants stopped performing training sessions, they were invited to complete post-training and follow-up assessment based on their last training session.

Data Analysis

Even though we had clear guidelines regarding the timing of these phases, there were deviations from protocol. Therefore, we will include the number of days between assessments and duration of training in the analyses. Furthermore, we did not exclude any data and did not handle missing data. Lastly, as registered on the Open Science Framework (osf.io/8ymd9), all analyses will be exploratory[1].

[1] At the time of writing this chapter for the dissertation, data collection is still ongoing. Therefore, the results displayed in the next section are preliminary, based on a large part of the data. Estimations are that we will have data on 378 participants; and that 200 participants will have completed the full protocol.

Results

Sample Characteristics

Sample characteristics are based on 311 participants that at least partially completed the baseline questionnaires. Age ranged between 18 and 72 years old, with a mean age of 41.8 years old (SD 12.9). Three quarters of the sample was female (227 female and 83 male, 1 non-binary) and thirty percent declared to use some medication for their mental health (95 used medication, 216 did not). Most participants were actively employed: 42% had a full-time job and 23% worked part-time. Furthermore, 10% were students and 11% was currently not working due to mental or physical health issues, either temporarily or permanently. The remainder of the sample was looking for a job (4%), retired (6%) or a homemaker (3%). Table 2 displays the scores for this group on questionnaires and naPASAT assessed during baseline. There is a lot of variability on these measures, as for most of the questionnaires the full possible range was obtained.

Training Adherence

As dropout during online psychological interventions is common, it was expected to occur in this study. Of the 311 participants that started baseline assessment, 246 participants completed this assessment. In this group, the majority completed all ten training sessions (157; 64%) and completed the naPASAT during post-training assessment (147; 60%). Complete data was obtained from 125 participants (40%). Dropout rates during the full protocol are described in Figure 1.

Table 2

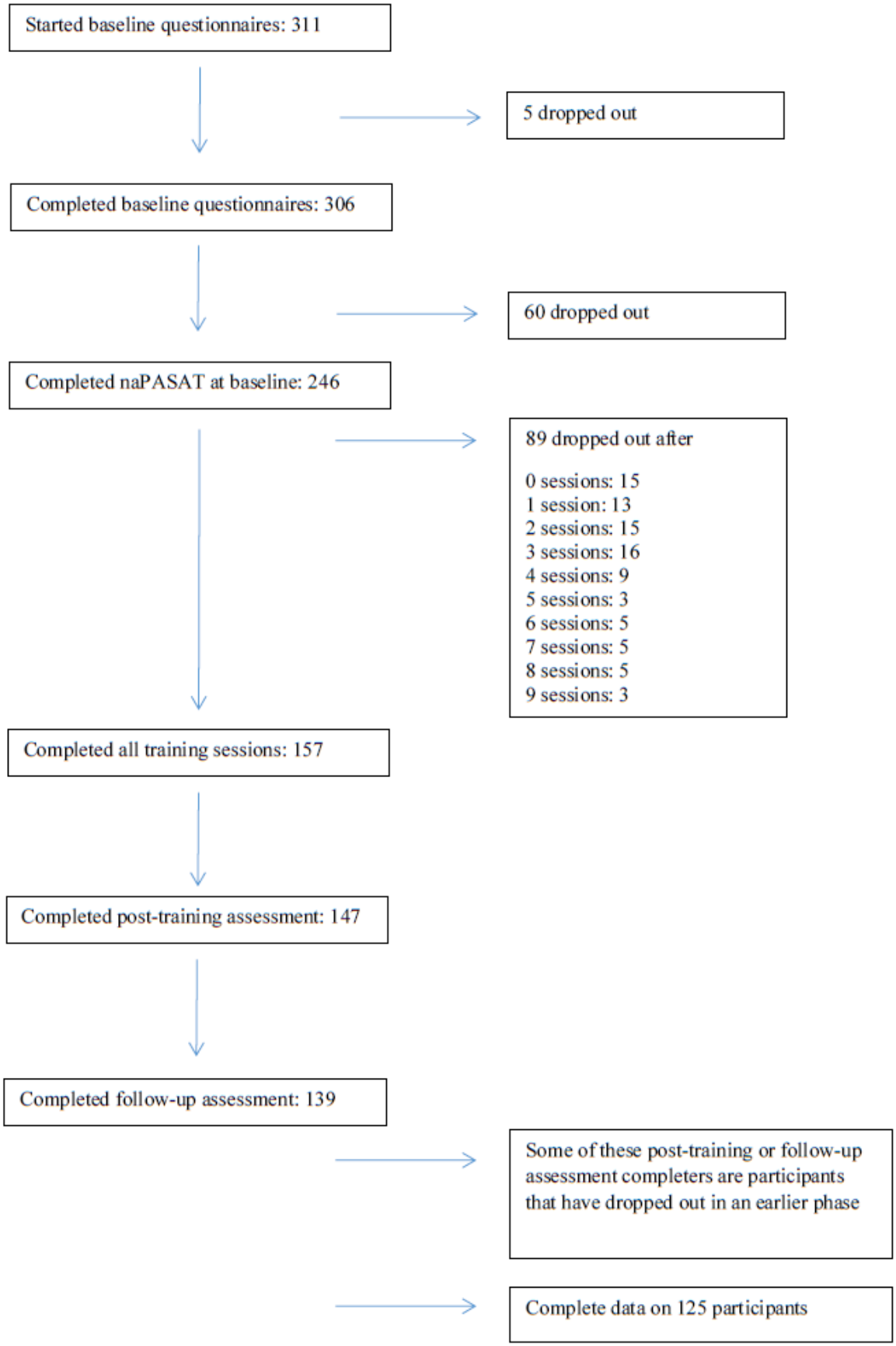
Sample Characteristics at Baseline Assessment

	N	Poss. Range	Obs. Range	Mean	SD
Trait Variables					
TIPI Extraversion	309	1-7	1-7	4.1	1.6
TIPI Agreeableness	309	1-7	2-7	5.4	1.0
TIPI Conscientiousness	309	1-7	1-7	5.0	1.3
TIPI Emotional Stability	309	1-7	1-7	3.5	1.4
TIPI Openness	309	1-7	1-7	5.0	1.5
RDQ Functioning	308	0-82	0-72	35.9	16.9
EC Activation Control	306	1-7	1.9-7	4.5	1.0
EC Attentional Control	306	1-7	1-6.6	3.8	1.0
EC Inhibitory Control	306	1-7	2.1-6.9	4.5	0.9
UES Engagement*	181	1-5	1.3-4.6	3.3	0.7
State Variables					
naPASAT Accuracy (%)	248	0-100	0-86.7	29.9	14.2
PTQ Core Characteristics	310	0-36	10-36	25.3	5.2
PTQ Unproductiveness	310	0-12	2-12	7.4	2.0
PTQ Mental Capacity	310	0-12	0-12	7.0	2.3
DASS Depression	308	0-42	0-42	13.3	5.0
DASS Anxiety	308	0-42	0-36	11.3	4.5
DASS Stress	308	0-42	0-42	19.4	4.8
ERQ Reappraisal	308	1-7	1-7	3.9	1.1
ERQ Suppression	308	1-7	1-6.8	3.4	1.4
CDRS Resilience	308	0-40	5-40	21.7	6.7

Poss. Range = possible range as defined in the questionnaire guidelines; Obs. Range = range of values observed in this sample; TIPI = Ten Item Personality Inventory; RDQ = Remission from Depression Questionnaire; EC = Effortful Control; UES = User Engagement Scale; naPASAT = non-adaptive Paced Auditory Serial Addition Task; PTQ = Perseverative Thinking Questionnaire; DASS = Depression Anxiety Stress Scales; ERQ = Emotion Regulation Questionnaire; CDRS = Connor-Davidson Resilience Scale

*: Engagement was measured during post-training assessment.

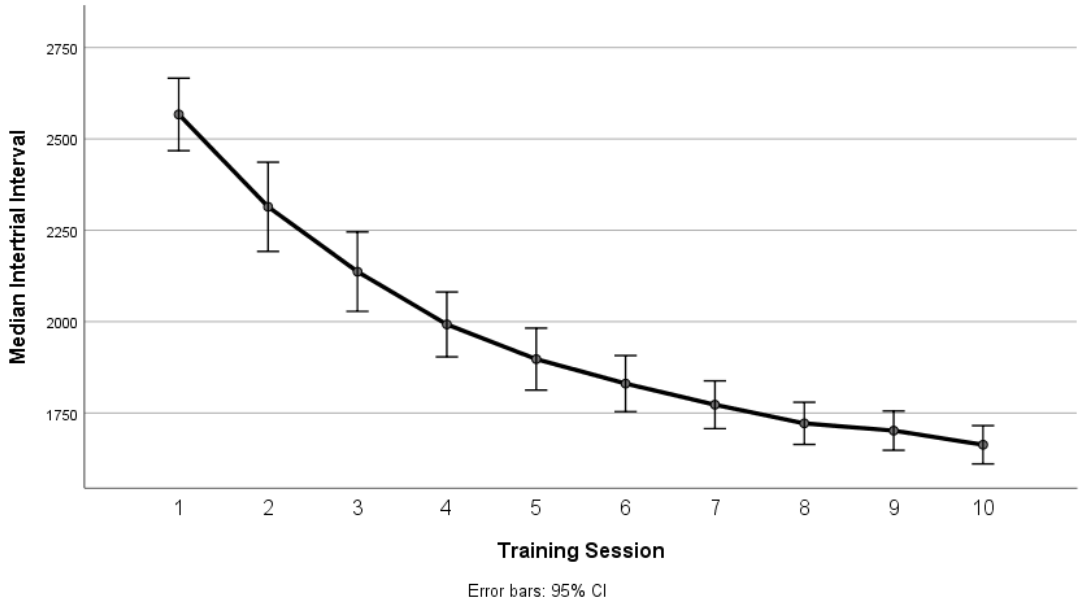
Figure 1. Flowchart of Participants



Training Progress

Progress during training was assessed using completers-only data. In total, 159 participants completed the training (2 participants completed training but not baseline assessment and were included here) and median intertrial intervals were calculated per session per subject. Conducting a Repeated Measures ANOVA with training session as a within-subjects factor with ten levels, indicated a significant effect of time [$F(2.5, 387.4) = 199.6$; $p < .001$; $\eta_p^2 = 0.558$]. Median intertrial intervals decreased over sessions, demonstrating that participants progressed in the training task (Figure 2).

Figure 2. Training Progress with Median Intertrial Interval per Session.

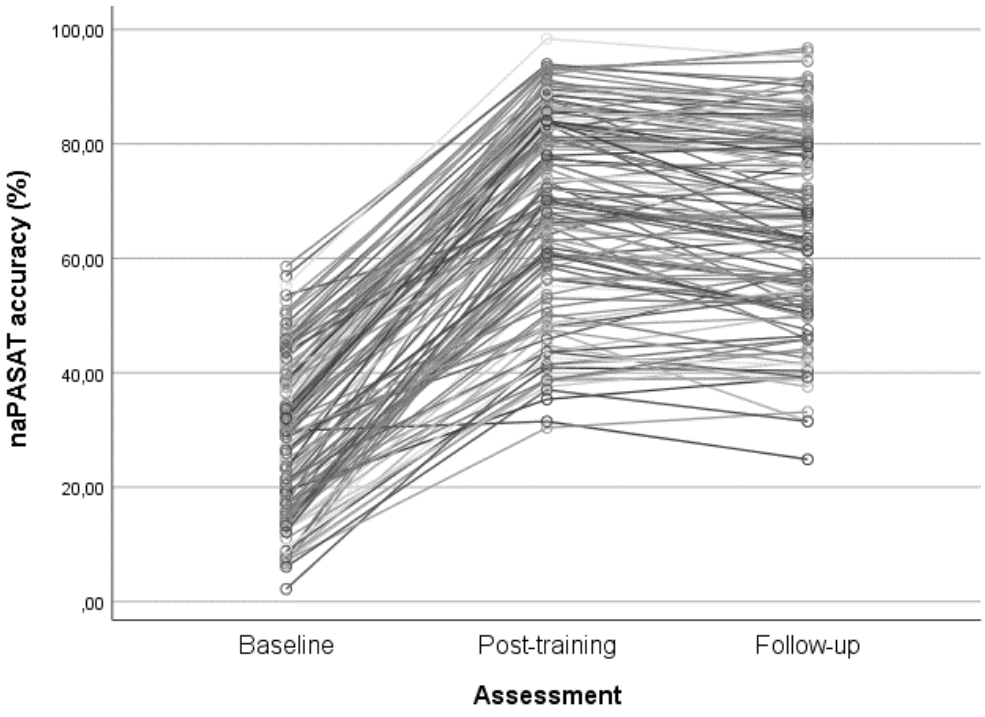


Progress on State Variables

In order to be able to look for moderators of training effectiveness, this training need to demonstrate some effects. Therefore, outcomes measures before and after training, and at follow-up were investigated, to ensure that the training showed expected effects. These analyses all consisted of completers-only Repeated Measures ANOVAs. Table 3 contains sample sizes and exact values.

naPASAT. Accuracy scores showed a strong improvement over time, [$F(1.5, 190.9) = 1146.0$; $p < .001$; $\eta_p^2 = 0.900$]. Follow-up paired samples *t*-tests showed a significant increase from baseline to post-training [$t(152) = 37.73$; $p < .001$; $d = 3.05$] and a decrease from post-training to follow-up assessment [$t(128) = 4.85$; $p < .001$; $d = 0.43$]. This pattern was highly consistent across participants, as illustrated by Figure 3. Accuracy on naPASAT will function as one of our two main outcome measures.

Figure 3. Spaghetti Plot of naPASAT Accuracy over Assessments.



PTQ. A decrease in RNT was observed in the three subscales separately, [Core characteristics: $F(2, 262) = 79.37$; $p < .001$; $\eta_p^2 = 0.377$; Unproductiveness: $F(1.9, 248.5) = 29.17$; $p < .001$; $\eta_p^2 = 0.182$; Mental load: $F(2, 262) = 30.52$; $p < .001$; $\eta_p^2 = 0.189$]. Follow-up paired samples *t*-tests showed a decrease from baseline to post-training assessment; and from post-training to follow-up assessment, for all three components [Baseline to post-training: Core characteristics: $t(180) = 8.67$; $p < .001$; $d = 0.64$; Unproductiveness: $t(180) = 5.00$; $p < .001$; $d = 0.37$; Mental load: $t(180) = 5.86$; $p < .001$; $d = 0.44$; Post-training to follow-up: Core characteristics: $t(131) = 5.73$; $p < .001$; $d = 0.50$; Unproductiveness: $t(131) = 3.54$; $p < .001$; $d = 0.31$; Mental load: $t(131) = 2.92$; $p < .001$; $d = 0.26$].

DASS. Following training, depressive, anxiety and stress symptomatology was reduced [Depression: $F(1.8, 233.4) = 22.15$; $p < .001$; $\eta_p^2 = 0.145$; Anxiety: $F(1.6, 209.6) = 36.00$; $p < .001$; $\eta_p^2 = 0.216$; Stress: $F(1.8, 240.4) = 26.18$; $p < .001$; $\eta_p^2 = 0.167$]. Follow-up paired samples *t*-tests revealed a significant decrease from baseline to post-training assessment for all subscales, but post-training and follow-up scores did not differ significantly [Baseline to post-training: Depression: $t(180) = 6.86$; $p < .001$; $d = 0.51$; Anxiety: $t(180) = 6.78$; $p < .001$; $d = 0.50$; Stress: $t(180) = 6.14$; $p < .001$; $d = 0.46$; Post-training to follow-up: Depression: $t(131) = 1.21$; $p = .228$; $d = 0.11$; Anxiety: $t(131) = 0.85$; $p = .394$; $d = 0.07$; Stress: $t(131) = 1.05$; $p = .295$; $d = 0.09$]. The depression subscale will serve as the second main outcome measure. However, as opposed to the accuracies on naPASAT assessments, these data did not show a consistent pattern across participants (Figure 4).

ERQ. Scores for the adaptive emotion regulation strategy Reappraisal showed increases over time [$F(1.9, 251.7) = 24.97$; $p < .001$; $\eta_p^2 = 0.160$]. In particular, scores increased from baseline to post-training assessment [$t(180) = 6.02$; $p < .001$; $d = 0.45$], but not from post-training to follow-up assessment[$t(131) = 1.13$; $p = .260$; $d = 0.10$]. Scores for the

maladaptive emotion regulation strategy Suppression did not change over time [$F(2, 262) = 2.30$; $p = .10$; $\eta_p^2 = 0.017$].

CDRS. Resilience also showed an increase over time [$F(2, 262) = 19.66$; $p < .001$; $\eta_p^2 = 0.130$]. Follow-up *t*-tests revealed a significant decrease from baseline to post-training assessment [$t(180) = 2.87$; $p = .005$; $d = 0.21$]; and from post-training to follow-up assessment [$t(131) = 2.92$; $p = .004$; $d = 0.25$].

Interim conclusion. The results from this data were similar to those of other CCT studies. Particularly, participants seemed to perform the training as instructed, as shown with progress and task-specific cognitive transfer, and there was evidence for beneficial effects overall (but there was no control condition). Scores showed a decrease in PNT and symptomatology and an increase in reappraisal and resilience.

Figure 4. Spaghetti Plot of Scores on DASS Depression Subscale over Assessments.

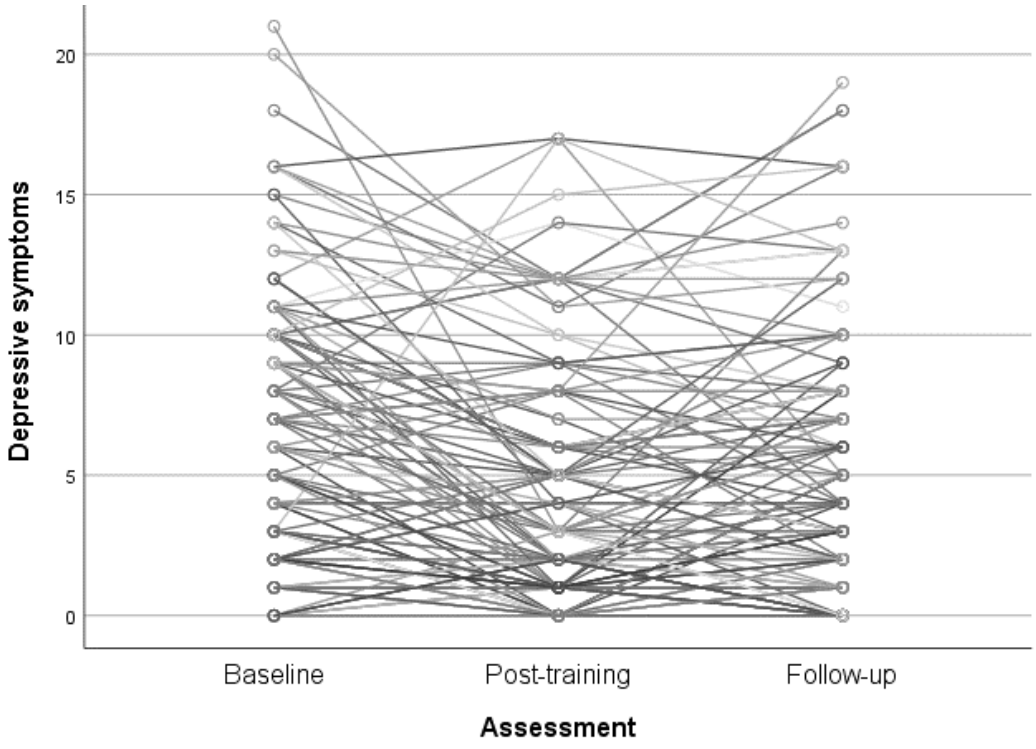


Table 3

Mean Scores over Repeated Assessments, with Standard Deviation in Parentheses

	Sample Size	Baseline Assessment	Post-training Assessment	Follow-up Assessment
NaPASAT (%)	129	29.46	69.09	66.14
		(13.69)	(17.10)	(16.81)
PTQ Core	132	25.25	22.20	20.08
		(4.92)	(5.76)	(5.66)
PTQ Unprod.	132	7.36	6.61	6.07
		(2.01)	(1.97)	(1.94)
PTQ Load	132	6.76	5.88	5.42
		(2.24)	(2.29)	(2.33)
DASS D	132	12.76	8.67	9.33
		(4.83)	(4.36)	(4.68)
DASS A	132	11.04	7.35	7.03
		(4.60)	(3.59)	(3.60)
DASS S	132	18.50	14.62	14.03
		(4.87)	(4.42)	(4.25)
ERQ Reap.	132	3.95	4.44	4.53
		(1.06)	(1.10)	(1.05)
ERQ Suppr.	132	3.32	3.16	3.20
		(1.43)	(1.36)	(1.26)
CDRS	132	21.83	23.18	24.22
		(6.40)	(6.07)	(6.04)

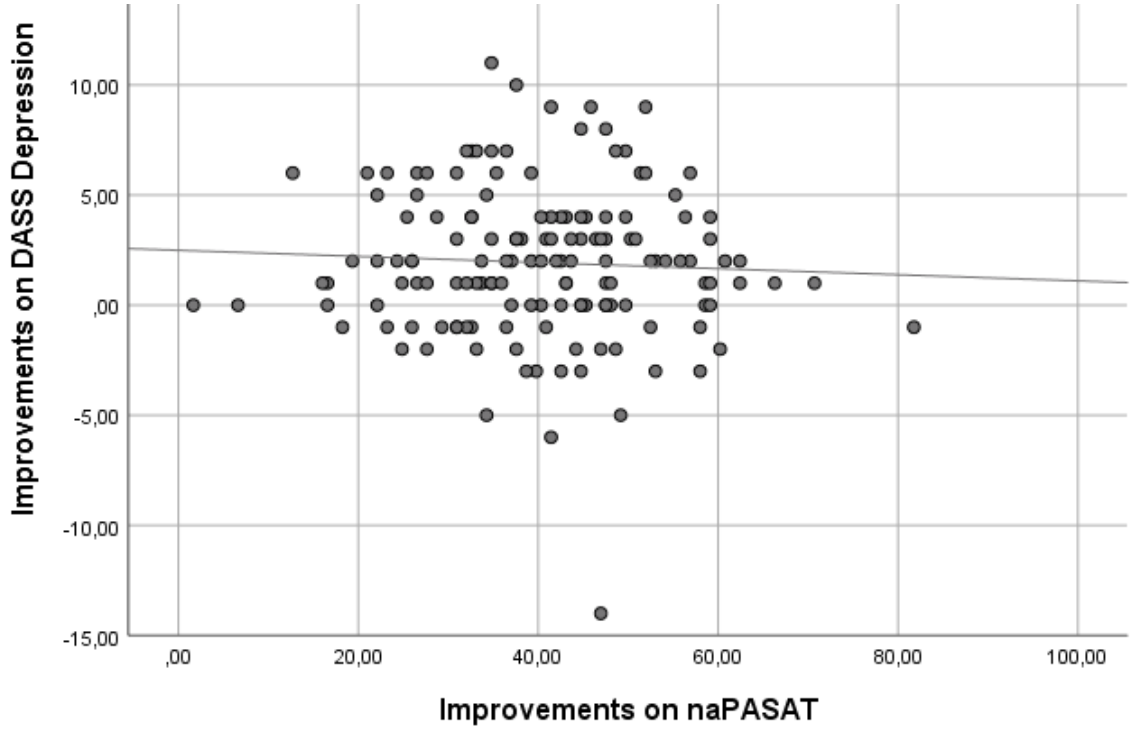
naPASAT = non-adaptive Paced Auditory Serial Addition Task; PTQ = Perseverative Thinking Questionnaire; Core = Core Characteristics; Unprod. = Unproductiveness; Load = Used mental capacity; DASS = Depression Anxiety Stress Scales; D = Depression; A = Anxiety; S = Stress; ERQ = Emotion Regulation Questionnaire; Reap. = Reappraisal; Suppr. = Suppression; CDRS = Connor-Davidson Resilience Scale

Identifying Predictors for Effectiveness

Our first main outcomes in terms of training effectiveness were improvement from baseline to post-training assessment in terms of naPASAT performance and depressive symptomatology as measured with the DASS depression subscale. Predictors for effectiveness will be explored. Given the explorative nature of this study, we will not correct for multiple comparisons. Our methodology is similar to the approach reported in Brunoni et al. (2014).

Characteristics of Training Outcomes. Performance on naPASAT showed a highly consistent pattern across participants (Figure 3), while the opposite was true for scores on the depression subscale of the DASS (Figure 4). Improvements from baseline to post-assessment on these two measures were not correlated [r = -0.052; p = .529] (Figure 5).

Figure 5. Scatter Plot of Improvements from Baseline to Post-Training Assessment.



Multiple linear regression analyses: baseline to post-training. As a first step, we computed two multiple linear regression models, one for each outcome measure. Possible predictors were all trait variables, thus demographics (age, gender, degree, employment, medication, math affinity and fear), personality (five dimensions), effortful control (three components), overall functioning and engagement. Furthermore, baseline scores on state variables were included, which were naPASAT accuracy, symptomatology (three subscales), RNT (three components), emotion regulation (two strategies) and resilience. Additionally, the number of completed training sessions was entered as well.

Improvement on naPASAT. Improvements in terms of naPASAT accuracy were significantly predicted by age, conscientiousness, engagement, core characteristics of RNT and naPASAT accuracy at baseline assessment, while depression scores at baseline was a marginal significant predictors (Table 4). This model explained 48.6% of total variance, as indicated by R^2. Higher engagement, more core characteristics of RNT and depressive symptomatology at baseline predicted larger improvements. Lower baseline naPASAT accuracy, less conscientiousness, and younger age predicted larger improvements.

Improvement on depressive symptomatology. Significant predictors for improvements in depressive symptomatology were math affinity, conscientiousness, engagement, activation control, and depressive symptomatology at baseline. Furthermore, use of the maladaptive emotion regulation strategy suppression was a marginal significant predictor (Table 4). This model explained 45.9% of total variance. Higher scores on conscientiousness, engagement and baseline depressive symptomatology predicted larger improvements. Less math affinity, activation control and use of suppression predicted larger improvements.

Some of these results seem counterintuitive, but might be due to floor and ceiling effects, as we sampled from a non-clinical population. Furthermore, some predictors were able to predict both outcome measures (conscientiousness, engagement and depressive symptomatology at baseline). However, the directionality of conscientiousness switched from one dependent variable to the other.

Table 4

Predictors for Improvements from Baseline to Post-Training Assessment.

	t	*p*	*B* (unstand.)	*Beta* (stand.)
Predictors for naPASAT improvement				
Age	2.14	.034	-0.268	-0.289
Conscientiousness	2.15	.034	-2.069	-0.194
Engagement	2.22	.028	3.330	0.166
RNT Core Baseline	2.43	.017	0.693	0.268
naPASAT Baseline	4.91	< .001	-0.398	-0.432
Depression Baseline*	1.70	.092	0.675	0.248
Predictors for DASS Depression improvement				
Math affinity	2.21	.029	-1.028	-0.185
Conscientiousness	2.64	.009	0.763	0.229
Engagement	1.98	.050	0.900	0.147
Activation Control	2.29	.023	-0.911	-0.234
Depression Baseline	5.64	<.001	0.605	0.751
Suppression Baseline*	1.71	.091	-0.411	-0.146

*: marginally significant

Multiple linear regression analyses: post-training to follow-up. As a second step, we computed two different multiple linear regression models, one for each outcome measure, but predicting improvements from post-training to follow-up assessment. Possible predictors were again all trait variables and baseline scores on state variables, as well as the number of completed training sessions. Additionally, post-training scores of naPASAT and DASS Depression were included as well. Importantly, although dependent variables here are framed as "improvements", there was actually a small deterioration from post to follow-up in terms of mean naPASAT accuracy and depression scores.

Improvement post to follow-up on naPASAT. This analysis resulted in a model that was able to explain 52.0% of the observed variance. Significant predictors were gender, math affinity, math fear, and naPASAT performance at baseline and post-training assessment. Furthermore, age, the mental load component of the PTQ during baseline assessment and the personality trait emotional stability were marginally significant predictors (Table 5). Larger improvements (or smaller declines) were predicted by being female, high fear of and high affinity with math, higher baseline and lower post-training scores on naPASAT, younger age, more RNT that is mentally loading at baseline and emotional stability.

Table 5

Predictors for Improvements from Post-Training to Follow-Up Assessment.

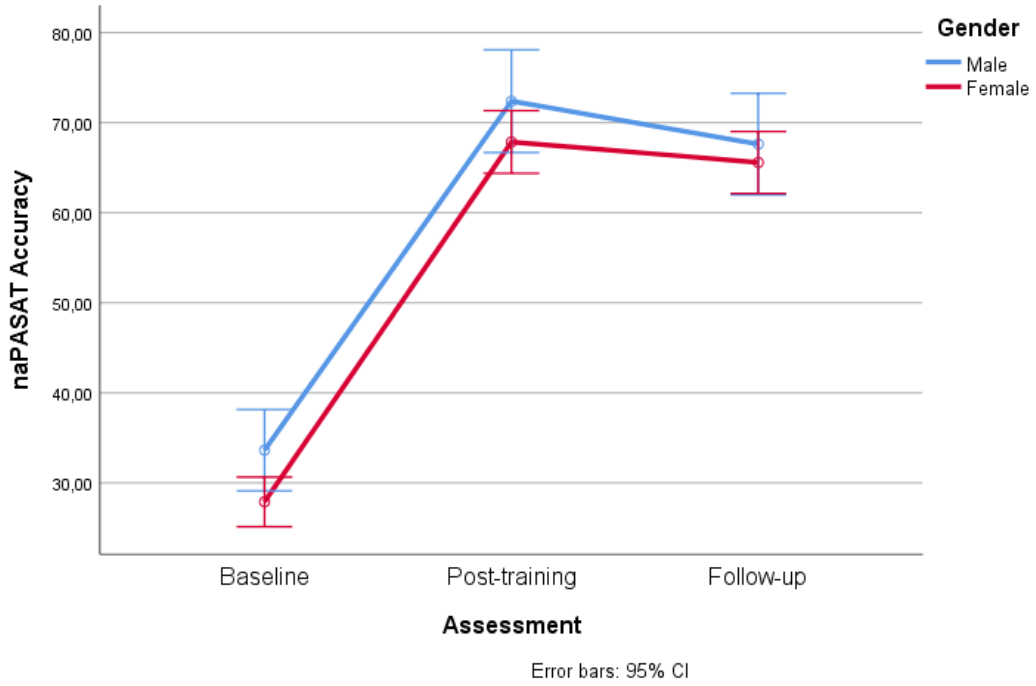
	t	*p*	*B* (unstand.)	*Beta* (stand.)
Predictors for naPASAT improvement				
Gender°	2.10	.038	-3.411	-0.225
Math Affinity	3.80	<.001	3.452	0.371
Math Fear	2.20	.031	1.505	0.215
naPASAT Baseline	5.50	< .001	0.379	0.768
naPASAT Post	5.57	<.001	-0.354	-0.892
Age*	1.80	.075	-0.144	-0.284
RNT Mental Load*	1.81	.074	0.786	0.260
Emotional Stability*	1.89	.063	1.022	0.212
Predictors for DASS Depression improvement				
Age	2.45	.016	-0.110	-0.460
Resilience Baseline	2.39	.019	0.172	0.342
Depression Post	2.31	.023	0.260	0.358
Attentional Control*	1.67	.098	0.721	0.217

°: 0 = female; 1 = male

*: marginally significant

To frame these findings regarding gender, males tended to have higher scores overall on naPASAT (Figure 6). Follow-up *t*-tests showed that this difference was marginally significant at baseline [$t(243) = 1.73$; $p = .085$; $d = 0.23$] but not significant during later assessments [post: $t(150) = 1.04$; $p = .300$; $d = 0.19$; follow-up: $t(138) = 0.70$; $p = .486$; $d = 0.13$]. For both genders, there was a significant decline in scores from post to follow-up [men: $t(34) = 4.77$; $p < .001$; $d = 0.82$; women: $t(93) = 3.08$; $p = .003$; $d = 0.32$], and this decline was somewhat steeper for men (this interaction was marginally significant: $F(1, 127) = 3.41$; $p = .067$; $\eta_p^2 = 0.03$) supposedly contributing to the significant effect of gender as a predictor. However, scores of men during follow-up assessment remained - non-significantly - higher than those of women; thus, this might denote merely a regression to the mean.

Figure 6. Performance on naPASAT over Assessments, per Gender.



Improvement post to follow-up on depressive symptomatology. Again, depressive symptomatology at baseline and naPASAT scores during post-training assessment were excluded from the model, which was able to explain 33.4% of variance but was not a significant improvement from the null model [$F(38, 122) = 1.11$; $p = .339$]. Age, resilience at baseline and depressive symptomatology during post-training assessment were significant predictors, and attentional control was a marginally significant predictor (Table 5). Remarkably, depressive symptomatology during baseline assessment was not a predictor [$t = 0.27$; $p = .788$]. Larger improvements were predicted by younger age, more resilience, higher depressive symptomatology at post-training assessment and more attentional control. This model was not better than a null model, and only explained a minor amount of variance. The large variability observed (Figure 4) cannot be explained by the variables included in the model.

Multivariate linear regression analysis. The second step in Brunoni et al. (2014) was to conduct a multivariate linear regression. Ideally, we would add all four main outcomes simultaneously as dependent variables (naPASAT pre-post and post-follow-up; and depressive symptoms pre-post and post-follow-up. However, entering post-training scores as predictors in the model (in addition to the baseline scores), would result in a perfect prediction for the outcomes regarding improvements from baseline to post. Therefore, two multivariate models were created instead: one model aiming to predict improvements from baseline to post-training without post-training scores, and another model pertaining improvements from post-training to follow-up with post-training scores as predictors. In these analyses, multicollinearity was not an issue (all variance inflation factors were less than 1.3).

Improvement baseline to post-training. All predictors identified in the previous step were entered in the model, except for post-training scores, namely age, gender, engagement, conscientiousness, emotional stability, activation control, attentional control, math affinity and math fear. Furthermore, baseline values for resilience, suppression, RNT core characteristics and mental load, naPASAT and DASS Depression were included. This model explained 35.1% and 29.9% of variance of the improvements on naPASAT and depressive symptomatology respectively. Multivariate testing showed a significant effect of age [$F(2, 130) = 13.88$; $p < .001$; $\eta_p^2 = 0.18$], engagement [$F(2, 130) = 4.35$; $p = .015$; $\eta_p^2 = 0.06$], conscientiousness [$F(2, 130) = 3.53$; $p = .032$; $\eta_p^2 = 0.05$], resilience [$F(2, 130) = 3.45$; $p = .035$; $\eta_p^2 = 0.05$], math affinity [$F(2, 130) = 3.22$; $p = .043$; $\eta_p^2 = 0.05$], naPASAT accuracy [$F(2, 130) = 13.71$; $p < .001$; $\eta_p^2 = 0.17$] and depressive symptomatology at baseline [$F(2, 130) = 13.99$; $p < .001$; $\eta_p^2 = 0.18$]. Parameter estimates are listed in Table 6.

Improvement post-training to follow-up. This model used the same set of predictors as the previous model, but also included post-training scores for naPASAT and DASS Depression. It explained 39.7% and 24.6% of improvements on naPASAT and DASS

Table 6.

Parameter Estimates of Multivariate Regression Models to Predict Improvement.

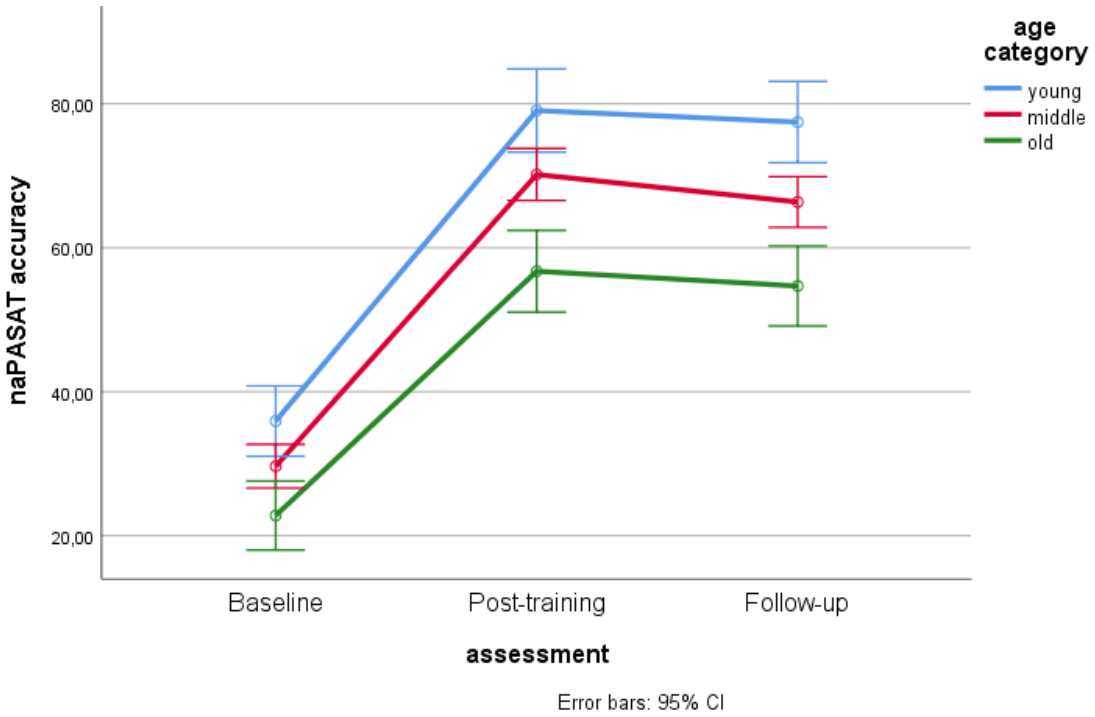
	B for naPASAT	B for depressive symptomatology
From baseline to post-training		
Age	-0.400	-0.028
Engagement	2.270	0.988
Conscientiousness	-1.741	0.472
Resilience baseline	-0.394	-0.074
Math affinity	3.373	-0.490
NaPASAT baseline	-0.402	0.012
DASS depr baseline	-0.170	0.352
From post-training to follow-up		
Gender°	3.782	-0.187
Math affinity	2.949	-0.598
naPASAT baseline	0.317	-0.010
naPASAT post	-0.304	-0.010
DASS depr. post	-0.098	0.291
Resilience baseline*	-0.102	0.133
Attentional control*	-0.884	0.772

°: 0 = female; 1 = male
*: marginally significant

Depression from post-training to follow-up assessment. Multivariate testing showed that gender [$F(2, 104) = 3.19$; $p = .045$; $\eta_p^2 = 0.06$], math affinity [$F(2, 104) = 5.99$; $p = .003$; $\eta_p^2 = 0.10$], baseline [$F(2, 104) = 15.51$; $p < .001$; $\eta_p^2 = 0.23$], and post-scores [$F(2, 104) = 16.46$; $p < .001$; $\eta_p^2 = 0.24$] on naPASAT were identified as significant predictors. Furthermore, post-scores on DASS Depression were significant [$F(2, 104) = 4.91$; $p = .009$; $\eta_p^2 = 0.09$], but baseline depressive symptoms was not [$F(2, 104) = 0.59$; $p = .556$; $\eta_p^2 = 0.01$]. Additionally, resilience [$F(2, 104) = 2.96$; $p = .056$; $\eta_p^2 = 0.06$] and attentional control [$F(2, 104) = 2.76$; $p = .068$; $\eta_p^2 = 0.05$] were marginally significant. Table 6 shows parameter estimates.

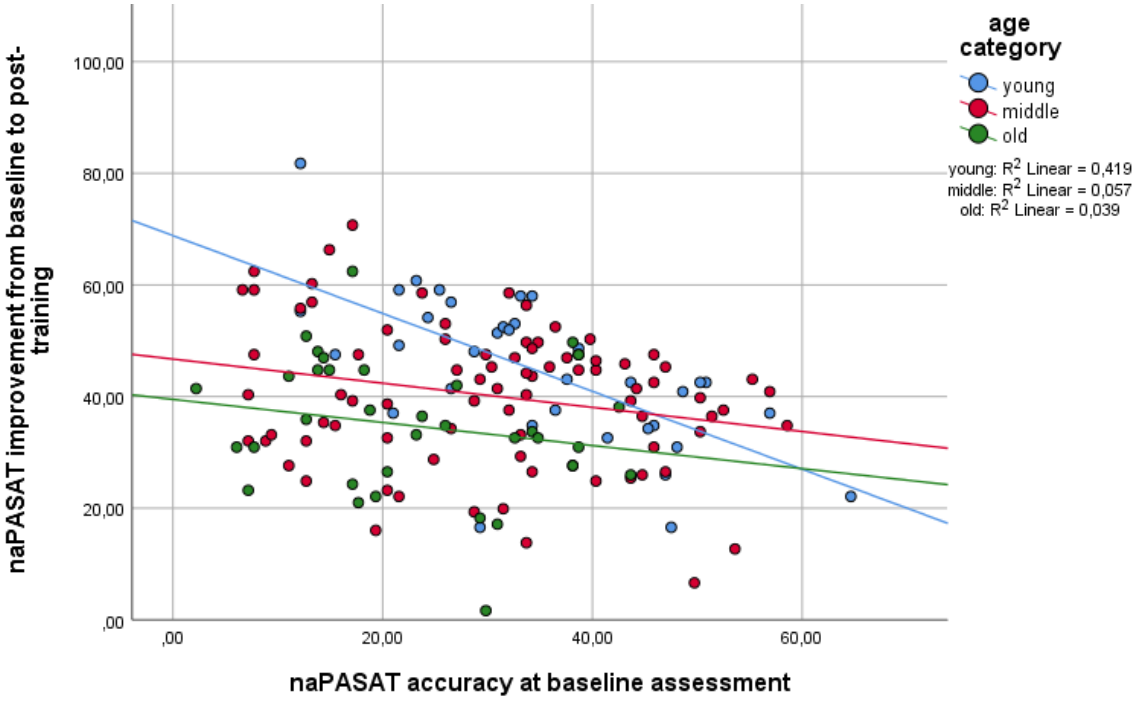
Relation age and cognitive control. As age frequently returns as a predictor for naPASAT accuracy, this relation was investigated further. Three categories were created based on age[2]: young (18-30 years); middle (31-55 years); and old (56-72 years). A Repeated Measures ANOVA with these categories as independent and naPASAT accuracy as dependent variable, across the three assessments, resulted in a significant interaction [F(3.0, 190.8) = 4.491; p = .004; η_p^2 = 0.07]. The young group showed elevated scores at baseline, and the differences between age groups increased over assessments, especially when naPASAT at baseline was low. This is illustrated further in Figures 7 and 8.

Figure 7. naPASAT Accuracy across Assessments, per Age Group.



[2] Changing the categories to 18-34; 35-54 and 55-72 years did not alter these results.

Figure 8. Relation between Age, naPASAT Accuracy at Baseline, and Improvement.



Conclusion regarding regression analyses. Overall, more variability was observed in depression scores than in naPASAT scores. Larger improvements from baseline to post-training scores (initial improvement) were consistently predicted by younger age, higher engagement scores and less resilience during baseline assessment. Larger improvements from post-training to follow-up assessment (stable improvement) were only predicted by lower scores on naPASAT during post-training assessment.

Discussion

Cognitive control training (CCT) has been utilized in past studies in the context of vulnerability for depression. A number of studies observed that CCT improved rumination and depressive symptoms, but the amount of empirical evidence is still limited (see Koster et al., 2017). Therefore, research into possible moderator variables is crucial.

This study provides a broad examination of potential moderators of CCT effects. A large and varied sample was administered CCT and key outcome variables were assessed before and after training, and one month later. Specifically as outcome variables we selected, repetitive negative thinking, depression, anxiety and stress symptomatology, emotion regulation and resilience. In general, after CCT most maladaptive processes were decreased and measures of adaptive processes and wellbeing increased. Although these findings are in line with previous research showing beneficial effects of CCT, our design did not include a control condition. Therefore, we cannot make strong claims about the specificity of CCT on these outcomes.

Furthermore, demographic variables, personality, effortful control, overall functioning and engagement were measured at one assessment and regarded as potential moderator variables in addition to the repeated measures at baseline assessment. Predicting improvements from baseline to post-training assessment on cognitive control task and in terms of depressive symptomatology, revealed significant effects of age, engagement, conscientiousness, and baseline scores for the cognitive control task, depressive symptomatology and resilience.

Using a select group of variables as predictors in a multivariate model to estimate improvement in scores of cognitive control and depression from post-training to follow-up assessment, resulted in significant effects of gender, and baseline and post-training scores for

the dependent variables (except for depression at baseline) and marginal effects for attentional control and resilience.

There was substantial variation in individual patterns observed in terms of depressive symptomatology, while the pattern for cognitive control task accuracy was more consistent. We were not able to explain the majority of variation using this selection of variables. Importantly, these two outcome measures were not correlated.

The finding of Brunoni et al. (2014) that age moderates CCT effects was found in this study as well. In this study, older participants profited less from CCT, which revealed an opposite pattern as the one in Brunoni et al. (2014). However, they applied CCT in combination with neuromodulation. A meta-analysis on cognitive training for depression, which included several CCT studies, showed that training effects decreased with age (Motter, Pimontel, Rindskopf, Devanand, Doraiswamy, & Sneed, 2016), which is in line with our findings. Furthermore, in line with the literature, older participants had worse baseline scores for cognitive control (Tombaugh, 2006). Interestingly, younger participants with lower cognitive control showed the largest improvements revealing a potential target group for CCT implementation.

Furthermore, engaged participants showed greater improvements from baseline to post-training assessment, confirming the finding of Siegle et al. (2014). Participants exhibiting less resilience at baseline improved more, which seems counterintuitive. However, low resilience can predict several vulnerability factors, including rumination, depressive symptomatology and cognitive complaints (Hoorelbeke et al., 2019), possibly identifying a subgroup that might profit from CCT. Additionally, lower cognitive control scores at post-training predicted improvement from post-training to follow-up. We believe that this might be due to regression to the mean in participants that show elevated scores at post-training for the cognitive task.

Conscientiousness was identified as a predictor for both outcome measures (cognitive control and depressive symptomatology) but in opposite directions. While higher scores on conscientiousness predicted smaller improvements on cognitive control, this predicted larger improvements in terms of depressive symptomatology. This finding cannot be readily explained. It is possibly that conscientious participants were more attentive during the tutorial of the cognitive control task during baseline assessment and understood it better, resulting in improved accuracy, as compared to a less attentive group. Furthermore, through training, instructions might become fully understood by this latter group, diminishing differences at post-training assessment. Regarding depressive symptomatology, conscientiousness can predict perfectionism (Stoeber, Otto, & Dalbert, 2009), offering a possible partial explanation for these results. However, this is highly speculative and should be tested in future studies.

Different predictors for outcomes at post-training assessment vs. at follow-up assessment might indicate that time of assessment is important, and changes in the time frame might lead to different results. We believe we found evidence that CCT is characterized by short-term effects, at least for some measures in a non-clinical sample, as overall, scores were diminished during follow-up assessment. However, Hoorelbeke and Koster (2017) showed stronger effects after three months, than immediately following training in a remitted depressed group. Future studies might investigate the time lapse of CCT effects.

To conclude, we found that age, engagement and resilience are important moderators of CCT effectiveness. Younger individuals profit more from CCT, especially when their cognitive control is low, and might be targeted in this context. Furthermore, better outcomes were found in highly engaged participants. Lastly, low resilience predicted improved outcomes. No other variables were consistently found in the broad range of measures we included to consistently predict outcomes.

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Chapter 7: General Discussion

Cognitive control impairments are thought to be an underlying mechanism in depression that forms a vulnerability factor for developing new depressive episodes in remitted patients. The past decade, cognitive control training has been deployed as a means to ameliorate these impairments, by administering tasks that recruit cognitive control frequently and repeatedly. By remediating these deficits, more control over content in working memory can be exerted, disrupting the vicious cycle of negative mood, behavior, and thinking. Indeed, beneficial effects of cognitive control training have been found, mainly in terms of improved cognitive functioning, and diminished depressive symptomatology and rumination. However, not all training studies have reported these effects. Importantly, these studies used a wide array of tasks and training implementations, but even within trainings relying on the same task divergent effects were observed. Thus, cognitive control training shows promising potential as a preventive intervention, but research on effectiveness remains crucial.

In recent years, the field of internet-based interventions for mental health has grown exponentially. Although this domain is appealing given its substantial reach and scalability without decreasing treatment effectiveness, the majority of users terminate interventions prematurely. Several factors have been identified that can impact dropout and treatment outcomes, such as therapist contact, engagement, expectation, and gamification. Currently, progress within this field has not been applied in the context of cognitive control training in remitted depressed patients, although cognitive control training could be implemented as an internet-based intervention.

The purpose of this thesis was to develop and implement a new cognitive control training tool, with improved user engagement and individualized treatment options, aimed at

remitted depressed individuals as a relapse prevention tool. The remainder of this chapter will provide a summarized overview of the results reported in the chapters throughout this thesis. Furthermore, implications for the broader field and their consequences will be discussed, along with some limitations. Lastly, directions for future research are proposed, followed by a general conclusion of this thesis.

Summary of Findings and Implications

A first step in developing new software targeted at a specific group, is mapping the experiences of and requirements for this group. To this aim, a focus group with remitted depressed individuals and interviews with mental health professionals were organized. Main results showed mandatory requirements for remitted depressed individuals in terms of training configuration, technological, as well as personal factors. In other words, training should be user-friendly and functional, allowing for flexibility in training schedule and location, and available on several devices without need for a strong technological background in users. Desirable requirements for this population were knowledge and enjoyment, meaning that understanding what the training aims to do and why this could result in beneficial effects, as well as offering an engaging and interesting experience could help increase uptake and adherence of this training tool. Mental health professionals possibly have constraints depending on their working environment as they might need approval from their supervisor, if applicable in their professional setting. Furthermore, investing time was an important issue. Lastly, knowledge and therapeutic benefits facilitate implementation of cognitive control training. If they understand the supposed mechanisms of this type of training and what the possible benefits are, they would offer it more easily.

Second, these requirements were taken into account during the development of the new software. We collaborated with a software developer from Flanders, and were able to test and

give feedback on the software throughout different stages of development. A pilot study with users from the target population (remitted depressed individuals) confirmed the added improvements and informed us with new suggestions. After finalizing the software, it needed to be implemented. In this thesis, we included three empirical studies with similar methodology, using the newly developed software.

These three studies included different samples (a convenience sample, a remitted depressed sample and self-identified worriers) and investigated different research aspects (cognitive transfer, clinical effects and moderators for effectiveness). As the first study showed no impact of gamification on training effectiveness, both gamification levels of training task could be implemented, depending on the purpose of the study. Over the three studies, we found beneficial effects of CCT as compared to an active control training: we found a decrease in anxiety, depressive and residual symptomatology, and increased effortful control after training, apart from consistent task-specific cognitive transfer and improvement during training. We found no evidence for adverse effects of CCT. Furthermore, on several occasions, hypothesized effects of CCT were absent. Given that in the moderator study, we found significant, beneficial effects on nearly all variables, but changes in questionnaire scores were generally no more than a few points, it is possible that the initial studies were underpowered. Indeed, the final study included over twice as many CCT completers. Although our sample sizes were based on previously reported effects of CCT (Hoorelbeke & Koster, 2017), we were less stringent in these samples compared to the sample that reported the effects, possibly allowing more variability in the data and more power needed to find CCT effects in a consistent manner.

Interestingly, this thesis found some evidence for the hypothesis that CCT effects are temporary. In the clinical study we conducted, effects were typically diminished at six months compared to three months after training. This was the case for all observed effects (cognitive

transfer, depressive symptomatology, residual symptomatology) and is in line with a recent CCT study. Looking one year following training, no differences were observed on any of the questionnaires measuring clinical outcome variables (Hoorelbeke, Van den Bergh, De Raedt, Wichers, & Koster, under review). More generally, a meta-analysis on cognitive training interventions for elderly individuals, showed effects lasting between three and six months following training (Kelly, Loughrey, Lawlor, Robertson, Walsh, & Brennan, 2014). In this study, authors claim that two factors might lengthen duration of effects: adaptivity of training and booster sessions. In the past, booster sessions have shown to be effective in several domains, including cognitive training, assertion training, parent training, couples training, resuscitation training, and a self-management intervention for diabetes (Cheng et al., 2012; Baggs & Spence, 1990; Eyberg, Edwards, Boggs, & Foote, 1998; Braukhaus, Hahlweg, Kroeger, Groth, & Fehm-Wolfsdorf, 2003; Mundell, Kennedy, Szostek, & Cook, 2013; Fan & Sidani, 2009). But, meta-analyses in other domains have shown no effects of booster sessions (e.g., Dowden, Antonowicz, & Andrews, 2003; Schwalbe, Oh, & Zweben, 2014). Whether or not additional booster sessions might prolong effects in the context of CCT for depression remains to be explored.

Another factor that might impact duration and size of effect is training dosage. This was consistently ten sessions of 15 minutes throughout this thesis, but number of trials differed depending on individual level. In a cognitive training for elderly individuals, completers showed increased effects compared to non-completers (Cheng et al., 2012). In a meta-analysis on physical training, several training characteristics, such as duration and intensity, impacted effects significantly (Borde, Hortobágyi, & Granacher, 2015). Indeed, in CCT for depression, limited training does not succeed in impacting cognitive functioning (Koster, Hoorelbeke, Onraedt, Owens, & Derakshan, 2017), increasing importance of administering adequate

dosage. However, what amount of training (in terms of number of sessions, trials per session, session duration or training frequency) can be regarded as sufficient, remains unclear.

Related to this, is the question whether a dose-response relationship exists. Zhang and colleagues (2019) did not find a dose-response relation in the context of computerized cognitive training in impaired elderly individuals in their meta-analysis, but only compared less than ten hours to more than thirty hours of training, and the quality of the included studies was poor. In the context of depression, evidence for a dose-response relationship has been found for physical therapy and the antidepressant venlafaxine hydrochloride (Dunn, Trivedi, & O'Neal, 2001; Dunn, Trivedi, Kampert, Clark, & Chambliss, 2005; Rudolph, Fabre, Feighner, Rickels, Entsuah, & Derivan, 1998). Given that we consistently administered the same amount of dosage, this thesis cannot answer this question. Nevertheless, in the moderator study endeavors were made to include participants that received lower dosage, but limited variability in dosage prevented us to answer this question. Furthermore, it is possible that the necessary dosage is related to certain characteristics and should be tailored to the individual. To this aim, we believe that for individuals with more severe cognitive control impairments, a higher training dosage might be necessary.

In terms of dropout, the newly developed training shows promise. In this thesis, dropout was limited in all studies conducted. Admittedly, in the moderator study without individual incentives, dropout rates were elevated compared to the other two studies, but still acceptable. Engagement was measured in all studies and showed acceptable to good ratings. Furthermore, during training we received only a minimal amount of questions, showing good usability of training. In total, 390 individuals completed all ten training sessions which shows that this training implementation shows enough flexibility and is feasible, due in part to collaborating with a software developer with knowledge regarding design, user experience and gamification.

We believe that including several aspects highlighted by Fleming et al. (2016) helped with increasing acceptability. As mentioned in the general introduction of this thesis, they argued for (1) user-centered approaches, (2) engagement via gamification methods, (3) collaboration and (4) rapid testing and implementation. We followed these guidelines for the first aspect by gathering input provided by remitted depressed individuals and mental health professionals, including this in the development stage and conduct a pilot test with early-stage software. Furthermore, training difficulty was set at an individualized level, based on cognitive control impairments and performance during training. Lastly, we developed two task version (low vs. high gamification) as individuals differed greatly in preferences in this matter. Ideally, we will let users choose what task version they prefer, given that we found no effect of task version on training effectiveness. These gamification elements were added to increase engagement as mentioned in their second aspect. Indeed, we found some evidence that these elements might result in increased engagement but these effects were limited. In order to increase engagement further, we have added interactive psychoeducation with multiple choice questions in the platform. Participants received also clear information regarding contacting technical support during training and enforced a working ethic of responding in a timely manner. We do not assume this to be as effective as therapist contact but it might yield similar beneficial effects. In order to comply with the third aspect of Fleming et al. (2016), the development phase consisted of a collaboration between researchers, software developers, remitted depressed individuals and mental health professionals. Lastly, an agile development approach was utilized to be able to give feedback during development in a rapid manner (for specific examples of an agile methodology in the development of internet-based interventions, see Jacobs & Graham, 2016).

Limitations

The current thesis had also several limitations. A first limitation relates to the involvement of the target population. The development and testing of software occurred with input from only a limited number of these individuals. User requirements analysis was based on five remitted depressed individuals, and the user testing during software development included seven individuals with a history of depression. Admittedly, both numbers are low and the statement that these individuals and their input would be representative for the whole target population is questionable. Increasing these numbers however, could decrease sample sizes in upcoming studies or introduce difficulties with recruiting a sufficient number of participants, as these are pooled from the same target population. Although our participants in general were highly motivated to collaborate on this project, they were frequently working fulltime jobs, which decreases their availability. This balancing exercise of resources, time and involvement is common in several user-centered methods (de Beurs, van Bruinessen, Noorman, Friele, & van Dulmen, 2017). Although these methods have several advantages (e.g., increased usability and credibility of an intervention, possibly leading to increased engagement, uptake and adherence), their process can be complicated. De Beurs et al. (2017) described three different processes of including target users during development of an internet-based intervention for mental health: expert–driven method, intervention mapping, and scrum. In the *expert-driven method*, researchers design, discuss and develop an intervention. Following these stages, it is tested among a few end-users. Thus, end-users are only involved during the final stages of development. Large alterations are not possible at this point. *Intervention mapping* starts with a needs assessment, and this assessment serves as a basis to develop the intervention objectives. To suit these objectives, intervention methods are selected and developed, and plans regarding implementation are made. This does allow iterative actions and user involvement throughout the project. *Scrum* refers to an agile

working principle, where frequent meetings between different stakeholders are organized. One of these meetings can be used for a user requirements analysis. In the example of de Beurs et al. (2017), researchers, end users, developers and mental health professionals originally planned to discuss progress on a weekly basis. However, as this was highly intense for all parties involved, frequency was lowered to meeting first every two and later every three weeks. Our approach in this project was a combination of intervention mapping, where we included users both during early development stages and in testing of software, and a scrum methodology, as we also included a thorough user requirements analysis. Regardless of specific methodology, user input during development is an involved process with several tradeoffs and should be well thought-out before starting a project.

A second limitation pertains to the involvement of the software developers. In order to be able to develop functional, aesthetically pleasing, and engaging software, collaboration with this partner is recommended. However, issues can be found when interests are not aligned and communication not clearly defined. It is difficult to involve a professional software partner optimally in a research context. Frequently, developers have contracts for a fixed amount of labor (in duration or in features) during a fixed time period with fixed end-goals at the beginning of a project, and this does not combine easily with a research project, consisting of several steps that inform the next one and that is guided by found results. For instance, during user testing, additional requests were made but implementing these was no longer possible within the current budget. Furthermore, a substantial amount of resources went into the flow and the back-end part of the platform (more than initially budgeted), leaving less resources for the gamification implementation. Lastly, when a contract ends, there often is no longer any support from developers. However, bugs are often discovered throughout the lifecycle of software and currently, we cannot tackle these. Of course, it is not reasonable to expect extended follow-up from developers, as they find themselves in a rapid-

changing environment with multiple projects. One way to keep developers involved in a project might be to think about commercializing software. However, when doing so, several concerns should be considered, such as ethical principles.

Thirdly, mental health professionals only received a minimal role in this project. Although emphasized their importance during the user requirements phase, they were hardly involved in the rest of the project. In order to recruit participants for the clinical and the moderator study, we contacted some clinicians but could not involve them in a systematic and intensive manner. Given the fact that therapist contact can have important impact on interventions on- and offline, we still believe clinicians can play a crucial role in dissemination of this type of training and should be included in such projects (for a review on how to include psychiatrists, please see Zhang & Ho, 2015).

Future Research Opportunities

There are several options for future research to follow-up or be informed by this thesis. In terms of cognitive control training, several research questions remain. Searching for moderators did not result in unambiguous findings and other potential variables might be explored, such as the role of contact during training and metacognitions. The impact of booster sessions in the context of CCT remains to be investigated. More insight regarding duration of effects, adequate training dosage and dose-response relationships might inform researchers to achieve more stable CCT effectiveness. In this thesis, we targeted remitted depressed individuals using a PASAT-based training. CCT might be used as an add-on intervention for the treatment of depression (for a review on this possibility, see Van den Bergh, Hoorelbeke, De Raedt, & Koster, 2018). Information regarding effectiveness of CCT in comorbid psychopathology is still lacking. Patients with several other mental disorders suffer from repeated negative thinking and cognitive control impairments. Future research

might aim to find evidence that CCT can be applied outside the context of depression. Another opportunity might compare effectiveness of PASAT-based CCT with CCT relying on different tasks. Currently, no theories are available that explain superior effects of PASAT-based CCT. Lastly, in general, this domain might benefit from theoretical frameworks hypothesizing CCT effects and their active mechanisms and moderators, which might guide future research, and this can generate on its own turn additional hypotheses to inform theoretical frameworks.

With the emergence of machine learning, this technique might be utilized in the context of CCT for depression as well. Given sufficient sample sizes, this might help identify individuals at risk for relapse, for whom training is more effective, for whom CCT will not be effective, and gain more insight into the large heterogeneity of effects reported frequently. The field of machine learning in the context of predicting depression is in its infancy, but some studies have been conducted so far. Machine learning methods have been applied to distinguish between depressed and healthy individuals based on psychophysiology (Hosseinifard, Moradi, & Rostami, 2013; Sun, Shinba, Kirimoto, & Matsui, 2016), predict the onset of depression in a general sample (Wang, Sareen, Patten, Bolton, Schmitz, & Birney, 2014; Nigatu, Liu, & Wang, 2016) and in a remitted sample (Wang, Patten, Sareen, Bolton, Schmitz, & MacQueen, 2013). Furthermore, attempts have been made to predict treatment response (for a meta-analysis, see Lee et al., 2018). Identify individuals at risk for recurrence and having knowledge on subgroups particularly benefitting from CCT, would enable a precise and fruitful application of CCT in clinical practice.

Guidelines for Future Research

Internet-based interventions show promise in the context of mental health prevention (for a review, see Ebert, Cuijpers, Muñoz, & Baumeister, 2017). Furthermore, engagement

remains a central aspect and more guidelines to maximize this have been published recently. Specifically, Karekla and colleagues (2019) proposed ten recommendations to improve engagement in internet-based interventions for chronical illness sufferers. They identified four dimensions to group recommendations: a priori theoretical planning (e.g., gamification), human-computer interaction (e.g., human contact), tailoring and targeting to user groups (e.g., assessing computer literacy) and active assessment of usage (e.g., metrics to monitor adherence). We claim that the field would profit from adopting these recommendations.

We highly recommend involving individuals from the target population and collaborating with software developers and clinicians, but want to inform fellow researchers of possible obstacles along this path. In this paragraph some practical guidelines based on our experience throughout this project are listed, and these are in accordance with Fleming et al. (2016). First, allow for sufficient time to involve target users in the very first phase. The more information gathered at this step, the more acceptance of an intervention will be increased. Possible hurdles can be identified early on, avoiding certain risks or problems. Listening and involving the target users also increases the fit of interventions in their daily life, elevating uptake and adherence. Second, clear and frequent communication with software developers is key. It is possible that they have no experience with research designs and procedures, and some terms occur in both academia and software development but might have a different meaning, for instance randomization. When in doubt, assume the worst and explain what is meant with a certain term, which can save time for all parties involved. Third, proposals for software candidates should be reviewed by researchers as a guideline and not as a contract. Things might and will change. For instance, timing in the proposal is an estimation and deadlines will more often than not be postponed. Indeed, we encountered some delays and have noticed from personal correspondence that this is not an isolated case. Anticipating delays in software development might help with planning research projects. Lastly, think

about long-term implementation of an intervention, before any software has been developed. You will need updates of software packages and will encounter bugs. Candidates for software development that include extended warranty periods might be particularly interesting in this regard, or considering a shift to commercial software might be desirable.

General Conclusion

The current thesis aimed to develop and implement a new software tool to offer cognitive control training to remitted depressed individuals. We believe that the software tool that has been created suits our purposes well, and even with some restrictions, are satisfied with the finalized software. Including remitted depressed individuals, clinicians and software developers in the creation of this software, deemed to increase usability and implementation prospects of this intervention.

The empirical studies showed small but beneficial effects of CCT, which is in line with multiple studies in the field. Furthermore, some evidence is found for temporal effects and a moderating effect of age and engagement, confirming findings in the literature. However, substantial variability was observed in the data and additional research on CCT effectiveness is warranted. Several opportunities for future research are stated, along with guidelines for future internet-based interventions for mental health in general. We hope this project can inspire and stimulate future research, and contribute to the prevention of depression.

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validation. *Journal of Epidemiology and Community Health, 68*(5), 418-424. https://doi.org/10.1136/jech-2013-202845

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Data Storage Fact Sheets

Data Storage Fact Sheet regarding Chapter 2

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2. Information about the datasets to which this sheet applies

* Reference of the publication in which the datasets are reported:
Vervaeke, J., Van Looy, J., Hoorelbeke, K., Baeken, C., & Koster, E. H. W. (2018). User Requirements for a Gamified Cognitive Control Training for Remitted Depressed Individuals. *Journal of Medical Internet Research: Serious Games*, *6*(2), e6. https://doi.org/10.2196/games.8609

* Which datasets in that publication does this sheet apply to?:
There is only one dataset in that publication.

3. Information about the files that have been stored

3a. Raw data

* Have the raw data been stored by the main researcher? [x] YES / [ ] NO
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- [x] responsible ZAP
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- [ ] other (specify): ...

3b. Other files

* Which other files have been stored?
- [ ] file(s) describing the transition from raw data to reported results. Specify: ...
- [x] file(s) containing processed data. Specify: The data is qualitative. These other files (NVivo) consist of (categories of) nodes (or labels) added to the raw data.
- [ ] file(s) containing analyses. Specify: ...
- [x] files(s) containing information about informed consent
- [ ] a file specifying legal and ethical provisions
- [x] file(s) that describe the content of the stored files and how this content should be interpreted. Specify: a readme.txt files explains the storage and content of stored data on the share of the research group.
- [ ] other files. Specify: ...

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Data Storage Fact Sheet regarding Chapter 4

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2. Information about the datasets to which this sheet applies

* Reference of the publication in which the datasets are reported:
Vervaeke, J., Hoorelbeke, K., Baeken, C., Van Looy, J., & Koster, E. H. W. (2019). Transfer and Motivation After Cognitive Control Training for Remitted Depression in Healthy Sample. *Journal of Cognitive Enhancement*, 1-13. https://doi.org/10.1007/s41465-019-00135-6

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3. Information about the files that have been stored

3a. Raw data

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[x] researcher PC
[x] research group file server
[x] other (specify): UGent share of the main researcher and on the Open Science Framework

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[x] main researcher
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[ ] other (specify): ...

3b. Other files

* Which other files have been stored?
- [ ] file(s) describing the transition from raw data to reported results. Specify: ...

- [x] file(s) containing processed data. Specify: the folder "processed data" contains several files with cleaned data and an SPSS script that describes how questionnaire scores were calculated
- [x] file(s) containing analyses. Specify: the folder "analyses" contains the SPSS script for the main analyses.
- [ ] files(s) containing information about informed consent. Specify: ...
- [x] a file specifying legal and ethical provisions. Specify: the file requesting ethical approval from the ethical committee of the Faculty
- [x] file(s) that describe the content of the stored files and how this content should be interpreted. Specify: The 'readme.txt' file contains a clear description of all stored files, data, syntax used for this study.
- [x] other files. Specify: preregistration that was made on the open science framework

* On which platform are these other files stored?
- [x] individual PC
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2. Information about the datasets to which this sheet applies

* Reference of the publication in which the datasets are reported:
Vervaeke, J., Hoorelbeke, K., Baeken, C., & Koster, E. H. W. (submitted to Cognitive Therapy and Research). Online Cognitive Control Training for Remitted Depressed Individuals: A Replication and Extension Study.

* Which datasets in that publication does this sheet apply to?:
There is only one dataset in that manuscript.

3. Information about the files that have been stored

3a. Raw data

* Have the raw data been stored by the main researcher? [x] YES / [ ] NO
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- [x] other (specify): UGent share of the main researcher

* Who has direct access to the raw data (i.e., without intervention of another person)?
- [x] main researcher
- [x] responsible ZAP
- [x] all members of the research group
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- [ ] other (specify): ...

3b. Other files

* Which other files have been stored?
- [x] file(s) describing the transition from raw data to reported results. Specify: Some manual data cleaning is described in change_log.docx. An R-script that calculates questionnaire scores is saved as vragenlijstdata.R.
- [x] file(s) containing processed data. Specify: Several excel and spss files contain the processed data.
- [x] file(s) containing analyses. Specify: There are several spss files with analysis syntax and output.
- [ ] files(s) containing information about informed consent
- [x] a file specifying legal and ethical provisions: documents sent to the medical ethical committee for approval.
- [x] file(s) that describe the content of the stored files and how this content should be interpreted. Specify: There is a readme.txt file that explains the structure of the data, and meaning of the several folders and files.
- [ ] other files. Specify: ...

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Data Storage Fact Sheet regarding Chapter 6

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3a. Raw data

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* On which platform are the raw data stored?
- [x] researcher PC
- [x] research group file server
- [x] other (specify): UGent share of the main researcher

* Who has direct access to the raw data (i.e., without intervention of another person)?
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3b. Other files

* Which other files have been stored?
- [x] file(s) describing the transition from raw data to reported results. Specify: There are 3 files describing the transformation from raw to processed data, in SPSS, for the questionnaire data.
- [x] file(s) containing processed data. Specify: There are SPSS files per assessment, and one large file containing this aggregated data as well as the training and PASAT data.

- [ ] file(s) containing analyses. Specify: ...
- [ ] files(s) containing information about informed consent
- [x] a file specifying legal and ethical provisions: documents sent to the medical ethical committee for approval and the approval we received.
- [ ] file(s) that describe the content of the stored files and how this content should be interpreted. Specify: ...
- [ ] other files. Specify: ...

* On which platform are these other files stored?
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- [x] research group file server
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Nederlandstalige Samenvatting

Ernstige depressieve stoornis is een zeer slopende en vaak voorkomende psychische stoornis, geassocieerd met aanzienlijk lijden en kosten. Hoewel verschillende evidence-based behandelingen beschikbaar zijn, blijven hervalpercentages problematisch, wat aangeeft dat de huidige behandelingen onvoldoende gericht zijn op onderliggende kwetsbaarheidsfactoren. Verstoringen in cognitieve controle kunnen inderdaad waargenomen worden bij depressieve personen (Snyder, 2013; Levens & Gotlib, 2010) en blijven aanwezig tijdens remissie (Semkovska et al., 2019). Deze problemen worden gezien als een risicofactor gezien hun voorspellende waarde voor nieuwe episodes, en populaties met een risico op depressie vertonen verminderde cognitieve controle (Levens & Gotlib, 2015; Paelecke-Habermann, Pohl, & Leplow, 2005; Joormann, 2004; Owens & Derakshan, 2013).

Effectieve emotieregulatie wordt verondersteld afhankelijk te zijn van cognitieve controle en problemen met cognitieve controle kunnen leiden tot maladaptieve emotieregulatie zoals ruminatie, wat ook een risicofactor is voor depressie (Just & Alloy, 1997; Roberts, Gilboa, & Gotlib, 1998; Kuehner & Weber, 1999). Bij depressie belemmeren cognitieve controletekorten vermoedelijk een doeltreffende verwijdering van negatieve inhoud uit het werkgeheugen, resulterend in een langdurige verwerking van deze negatieve informatie, aanhoudende negatieve stemming, ruminatie en depressieve klachten (Joormann & D'Avanzato, 2010; Zetsche & Joormann, 2011; Koster , De Lissnyder, Derakshan, & De Raedt, 2011).

Verstoringen van de cognitieve controle kunnen worden verbeterd door het toepassen van cognitieve controle training (CCT), waarbij individuen herhaaldelijk en frequent, cognitieve controle gebruiken bij taken. Door de cognitieve controle te verhogen, kan meer

controle over de inhoud van het werkgeheugen worden uitgeoefend, waardoor de ruminerende gedachten afnemen wat resulteert in een minder depressieve gemoedstoestand. Er zijn inderdaad gunstige effecten van CCT tijdens depressie en remissie gevonden, in termen van cognitief functioneren, ruminatie en depressieve symptomatologie (e.g., Siegle, Ghinassi, & Thase, 2007; Hoorelbeke & Koster, 2017). Verschillende taken kunnen worden gebruikt voor CCT, maar de Paced Auditory Serial Addition Task (PASAT, Gronwall, 1977; Siegle et al., 2007) is de meest grondig onderzochte taak en is daarom doorheen dit proefschrift gebruikt.

Traditionele evidence-based behandelingen zijn geassocieerd met verschillende barrières, resulterend in een ruime groep onbehandelde patiënten (i.e., de treatment gap). Om die reden vindt er een verschuiving plaats naar interventies die gebruik maken van het internet. Deze interventies hebben verschillende voordelen, zoals een groter bereik, schaalbaarheid en kosteneffectiviteit. Belangrijk is dat deze interventies net zo effectief kunnen zijn als hun traditionele tegenhangers. Echter, een van de grootste uitdagingen in deze context is de lage therapietrouw en -adoptie, en de hoge uitval. Verschillende richtlijnen zijn voorgesteld om hiermee om te gaan (e.g., Fleming et al., 2016; Karekla et al., 2019) en moeten worden gevolgd tijdens de ontwikkeling van een internetinterventie.

Dit proefschrift presenteert een ontwikkeling en implementatie van een cognitieve controle training als een hulpmiddel voor hervalpreventie voor voorheen depressieve personen. Verschillende richtlijnen werden gevolgd om een boeiende, bruikbare en acceptabele training te garanderen, zonder vermindering van effectiviteit. Verder werd deze trainingstool empirisch onderzocht in een aantal verschillende studies.

Een eerste stap bij het ontwikkelen van nieuwe software gericht op een specifieke groep, is het in kaart brengen van de ervaringen van en vereisten voor deze groep. Hiertoe werd een focusgroep met voorheen depressieve personen en interviews met experten uit de

geestelijke gezondheidszorg georganiseerd. De belangrijkste resultaten waren dat training gebruiksvriendelijk en functioneel moet zijn, zodat flexibiliteit in trainingsschema en -locatie mogelijk is, en beschikbaar moet zijn op verschillende apparaten zonder dat er een sterke technologische kennis voor gebruikers nodig is. Gewenste vereisten voor voorheen depressieve personen waren kennis en plezier, wat betekent dat het begrijpen van het trainingsdoel en een boeiende en interessante ervaring hebben, de adoptie en therapietrouw van deze trainingstool zouden kunnen helpen verbeteren. Experten in de geestelijke gezondheidszorg gaven slechts beperkte mogelijkheden aan om tijd te investeren in online behandelingen naast de standaardbehandelingen. Kennis en therapeutische voordelen vergemakkelijken de implementatie van cognitieve controletraining. Als ze de veronderstelde mechanismen van dit soort training begrijpen en weten wat de mogelijke klinische voordelen zijn, zouden ze het gemakkelijker aanbieden.

Ten tweede, met deze vereisten werd rekening gehouden bij de ontwikkeling van de nieuwe software, samen met internationale richtlijnen voor internetinterventies. We werkten samen met een softwareontwikkelaar uit Vlaanderen en konden de software gedurende de verschillende fases van ontwikkeling testen en voorzien van feedback. Een pilotstudie met gebruikers uit de doelgroep (voorheen depressieve individuen) bevestigde de toegevoegde verbeteringen en voorzag ons met nieuwe suggesties. Nadat de software was voltooid, moest deze worden geïmplementeerd. In dit proefschrift hebben we drie empirische studies met vergelijkbare methoden opgenomen, met behulp van de nieuw ontwikkelde software. In alle studies bestond CCT uit tien sessies van adaptieve PASAT gedurende vijftien minuten, die over een periode van twee weken zouden moeten worden voltooid.

De eerste studie testte de impact van CCT, in vergelijking met een actieve controleconditie, en de impact van gamificatie (laag vs. hoog), op cognitieve en emotionele transfer, in een convenience sample. Hiertoe voltooiden 147 deelnemers twee cognitieve

taken (gestandaardiseerde PASAT en dual n-back taak) en vragenlijsten tijdens de baselinemeting en tijdens een post-training meting. Verder werd de engagement na de training bevraagd. De resultaten toonden een sterk taak-specifiek transfereffect van CCT (PASAT) maar geen far transfereffect (dual n-back taak). Bovendien had gamificatie geen invloed op beide types cognitieve transfer. Deelnemers die de taakversie met hoge gamificatie kregen, rapporteerden hogere scores voor engagement en motivatie. Ten slotte was er geen emotionele transfer van CCT in deze sample, maar angstsymptomatologie na de training leek verminderd te zijn, enkel in de CCT-groep met hoge gamificatie.

De tweede empirische studie onderzocht een steekproef van 68 voorheen depressieve patiënten, gerandomiseerd over CCT vs. actieve controleconditie. Deze studie diende als een replicatie en uitbreiding van Hoorelbeke en Koster (2017), die gunstige effecten van CCT aantoonde bij remitterende depressieve personen, tot drie maanden na de training. In ons onderzoek waren evaluaties gepland vóór en na de training, en na drie en zes maanden follow-up, wat dus de opvolgperiode verlengde. CCT vertoonde een sterk taak-specifiek cognitief transfereffect en een afname van depressieve symptomatologie bij sommige maten. Verder waren we in staat om de gunstige resultaten in termen van resterende symptomatologie te repliceren met exploratieve analyses, die tijdelijke effecten van CCT onthulden, die verminderd waren bij de laatste opvolgmeting. Niet alle oorspronkelijke bevindingen konden echter worden gerepliceerd.

Een laatste studie zocht naar moderatoren van effectiviteit bij CCT. Hiervoor werd een grote steekproef van 311 zelf geïdentificeerde piekeraars gerekruteerd voor deze studie, die volledig online verliep. Alle deelnemers ontvingen de gegamificeerde versie van CCT. Er waren drie meetmomenten: voor en na de training, en een maand later. Een breed scala aan potentiële moderators werd beoordeeld, waaronder demografische variabelen, persoonlijkheid, globaal functioneren, effortful controle, cognitieve controle, repetitief

negatief denken, depressieve, angst- en stresssymptomatologie, veerkracht en engagement. Bijna alle variabelen die meerdere keren werden gemeten, vertoonden gunstige effecten van training. Wat moderatoren betreft, was leeftijd in staat om CCT-resultaten te voorspellen, waarbij jongere mensen meer nut hadden van training, vooral wanneer de cognitieve controle laag was tijdens de baselinemeting. Bovendien vertoonden zeer geëngageerde en minder veerkrachtige individuen grotere verbeteringen.

Dit proefschrift liet zien dat het implementeren van richtlijnen met betrekking tot op internetinterventies haalbaar is en kan leiden tot een goed ontvangen interventie. Bovendien zijn de klinische effecten in overeenstemming met de huidige literatuur met betrekking tot CCT. In het bijzonder werden gunstige effecten gevonden, maar niet op een consistente wijze, terwijl er geen nadelige effecten van CCT werden waargenomen. Over het algemeen hebben we aanzienlijke variabiliteit waargenomen tussen verschillende onderzoeken en individuen. Aangezien gunstige effecten consistenter werden waargenomen in het laatste onderzoek met een grotere steekproef, zouden toekomstige CCT-onderzoeken kunnen overwegen om de steekproef te vergroten om de power te verhogen. Bovendien lijkt CCT kortetermijnseffecten te vertonen, die afnemen tijdens de maanden na de training, waar het interessant kan zijn om de impact van boostersessies na te gaan. Hoe het effect van CCT tijdens de periode na de training fluctueert, is momenteel onduidelijk. Tot slot gaven we verschillende suggesties voor toekomstig onderzoek naar CCT in de context van depressie.

English Summary

Major depressive disorder is a highly debilitating and common mental disorder, associated with substantial suffering and costs. Although several evidence-based treatments are available, recurrence rates remain problematic, indicating that current treatments do not target underlying vulnerability factors sufficiently. Indeed, cognitive control impairments can be observed in depressive individuals (Snyder, 2013; Levens & Gotlib, 2010), and remain present during remission (Semkovska et al., 2019). These impairments are considered a risk factor given their predictive value for new episodes, and populations at risk for depression have demonstrated impairments of cognitive control (Levens & Gotlib, 2015; Paelecke-Habermann, Pohl, & Leplow, 2005; Joormann, 2004; Owens & Derakshan, 2013).

Effective emotion regulation is thought to rely on cognitive control and problems with cognitive control can result in maladaptive emotion regulation such as rumination, which is a risk factor for depression as well (Just & Alloy, 1997; Roberts, Gilboa, & Gotlib, 1998; Kuehner & Weber, 1999). In depression, cognitive control deficits supposedly hinder effective removal of negative content from working memory, resulting in prolonged processing of this negative information, sustained negative mood, rumination and depressive complaints (Joormann & D'Avanzato, 2010; Zetsche & Joormann, 2011; Koster, De Lissnyder, Derakshan, & De Raedt, 2011).

Cognitive control impairments can be ameliorated by applying cognitive control training (CCT), where individuals recruit cognitive control repetitively and frequently, in tasks. By increasing cognitive control, more control can be exerted over content in working memory, decreasing ruminative thoughts and resulting in less depressive mood. Indeed, beneficial effects of CCT during depression and remission have been found, in terms of

cognitive functioning, rumination and depressive symptomatology (e.g., Siegle, Ghinassi, & Thase, 2007; Hoorelbeke & Koster, 2017). Several tasks can be used for CCT, but the Paced Auditory Serial Addition Task (PASAT, Gronwall, 1977; Siegle et al., 2007) is the most thoroughly investigated task and has therefore been used throughout this thesis.

Traditional evidence-based treatments are associated with several barriers, resulting in an ample group of patients left untreated (i.e., the treatment gap). Therefore, a shift to internet-based interventions is occurring. These interventions have several advantages, such as an increased reach, scalability, and cost-effectiveness. Importantly, these interventions can be as effective as their traditional counterparts. However, one of the biggest challenges in this context refers to low adherence and uptake, and high dropout rates. Several guidelines have been proposed to tackle these (e.g., Fleming et al., 2016; Karekla et al., 2019) and should be included during development of an internet-based intervention.

This thesis presents a development and implementation of a cognitive control training as a relapse prevention tool for remitted depressed individuals. Several guidelines were followed to ensure an engaging, usable and acceptable training, without decreasing effectiveness. Furthermore, this training tool was empirically investigated in a number of different studies.

A first step in developing new software targeted at a specific group, is mapping the experiences of and requirements for this group. To this aim, a focus group with remitted depressed individuals and interviews with mental health professionals were organized. Main results showed that training should be user-friendly and functional, allowing for flexibility in training schedule and location, and available on several devices without need for a strong technological background in users. Desirable requirements for remitted depressed individuals were knowledge and enjoyment, meaning that understanding the training goal and an engaging and interesting experience could help increase uptake and adherence of this training

tool. Mental health professionals showed only limited possibilities for investing time in online treatments next to the standard treatments. Knowledge and therapeutic benefits facilitate implementation of cognitive control training. If they understand the supposed mechanisms of this type of training and what the possible clinical benefits are, they would offer it more easily.

Second, these requirements were taken into account during the development of the new software, together with international guidelines regarding internet-based interventions. We collaborated with a software developer from Flanders, and were able to test and give feedback on different stages throughout software development. A pilot study with users from the target population (remitted depressed individuals) confirmed the added improvements and informed us with new suggestions. After finalizing the software, it needed to be implemented. In this thesis, we included three empirical studies with similar methodology, using the newly developed software. In all studies, CCT consisted of ten sessions of adaptive PASAT for fifteen minutes, that should be completed over a period of two weeks.

The first study tested the impact of CCT, compared to an active control condition, and the impact of gamification (low vs. high), on cognitive and emotional transfer, in a convenience sample. To this aim, 147 participants completed two cognitive tasks (standardized PASAT and dual n-back task) and questionnaires during baseline assessment and during post-training assessment. Furthermore, engagement was assessed following training. Results showed a strong task-specific transfer effect of CCT (PASAT) but no far transfer effect (dual n-back task). Furthermore, there was no impact of gamification on either cognitive transfer. Participants that received the high gamification task versions reported higher scores for engagement and motivation. Lastly, there was no emotional transfer of CCT in this convenience sample, apart from some evidence for decreased anxiety symptomatology after training, in the CCT group with high gamification only.

The second empirical study investigated a sample of 68 remitted depressed patients, randomized over CCT vs. active control condition. This study served as a replication and extension of Hoorelbeke and Koster (2017), that showed beneficial effects of CCT in remitted depressed individuals, up to three months following training. In our study, assessments were scheduled before and after training, and at three and six months follow-up, extending the follow-up period. CCT showed a strong task-specific cognitive transfer effect and a decrease in depressive symptomatology on some measures. Furthermore, we were able to replicate the beneficial results in terms of residual symptomatology with exploratory analyses, which revealed temporary effects of CCT that were diminished during the final follow-up assessment. However, not all original findings were replicated.

A final study searched for moderators of effectiveness of CCT. To this aim, a large sample of 311 self-identified worriers was recruited for this fully online study. All participants received the high gamification version of CCT. There were three assessments: before and after training, and one month after training. A broad variety of potential moderators was assessed, including demographic variables, personality, general functioning, effortful control, cognitive control, repetitive negative thinking, depressive, anxiety and stress symptomatology, resilience and engagement. Nearly all measures that were assessed multiple times showed beneficial effects of training. In terms of moderators, age was able to predict CCT outcomes, with younger age benefiting more from training, especially when cognitive control was low during baseline assessment. Furthermore, highly engaged and less resilient individuals showed larger improvements.

This thesis showed that implementing guidelines regarding internet-based interventions is feasible, and can lead to a well-received intervention. Furthermore, clinical effects are in line with current literature regarding CCT. Specifically, beneficial effects were found but not in a consistent manner, while no adverse effects of CCT were observed. Overall, we observed

substantial variability over different studies and individuals. Given that beneficial effects were observed more consistently in the final study with a larger sample size, future CCT studies could consider increasing sample size to increase power. Furthermore, CCT seems to demonstrate short-term effects, that decrease during the months following training, where effects of booster sessions might be interesting to pursue. How CCT impact fluctuates during the post-training time period is currently unclear. Lastly, we offered several suggestions for future research regarding CCT in the context of depression.

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