Reducing daily stress: Breaking a habit

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“People are not disturbed by things, but by the view they take of them”
Epictetus

General introduction

01

STRESS

Experiencing stressful events throughout your life can seem as inevitable as death and taxes. Yet the extent to which an individual experiences psychological strain due to these stressful events or stressors varies. It is generally assumed that individuals experience psychological strain when they evaluate situations as either threatening or taxing, and when they consider their coping resources to be insufficient [1, 2]. The list of potential stressors is inexhaustible and includes, for instance, marital conflict, death of a relative, financial hardship, and social isolation.

The most frequently studied stressful event is work stress. This is not surprising as concerns about work stress appear to be on the rise and work stress has even been considered a modern day epidemic [3]. Specifically, it has been argued that recent major changes in the workplace have put increasing demands on employees [3, 4]. One such change relates to the rapid technological progress of the past four decades with the development of the computer, Internet, and smartphones. These developments have provided unlimited communication possibilities, but have put employees at risk by enabling them to maintain nonstop contact with work and to work at any moment, anytime [3]. Indeed, throughout Europe, increases in job demands have been observed [5, 6]. Furthermore, these reports indicate increases in workload, time pressure, job insecurity, and decreases in job control. These factors are recognized to be important sources of stress [7]. Notably, stress is the second most commonly reported work-related health problem and 22% of the Europeans experience work stress [6]. In the Netherlands one third of the employees indicate that work load and work stress are the main reason for their recent work-related absence [8]. Moreover, the annual costs for Dutch employers of this work stress related absenteeism is estimated to be 1.8 billion Euros [9]. Stress is thus both highly prevalent and costly for society.

STRESS AND HEALTH

In response to challenges in the environment—whether it concerns daily hassles or major life events—the human body protects itself by activating the necessary physiological systems such as the autonomic nervous system (ANS) and the hypothalamic-pituitary-adrenal (HPA) axis [10, 11]. Changes in such physiological systems allow the body to deal with stressful situations. For example, heart rate and blood pressure are elevated through the release of catecholamines, which ensures that the body has sufficient oxygen and nutrients to undertake action (e.g., flee from the stressful situation). Once the stressor has past, the activated physiological systems

are deactivated and are returned to their normal level of activity. This process is called 'allostasis' and is considered useful as it helps individuals adapt to the environment [10, 11]. However, these adaptive physiological responses can strain the body through repeated activation or when the physiological response persists after the stressor is gone (resulting in prolonged exposure to stress-related physiological activity). In short, frequent and prolonged stress can cause chronic overactivity or dysregulation in the allostatic systems, and this in turn has a negative effect on both mental health [11-15] and physical health [12, 16, 17], including cardiovascular health [18-24].

To illustrate, in a large-scaled case control study with patients with a first myocardial infarction and controls, Rosengren et al. [23] showed that experiencing *some* stress at work or in general (i.e., defined as either stress at work or at home) was associated with increased odds of acute myocardial infarction with 1.38 and 1.45, respectively. Moreover, experiencing *continuing* stress increased the odds more than two-fold. Two meta-analyses [21, 22] describe similar increased risks for cardiovascular disease (CVD) when individuals report experiencing job strain or work stress. Importantly, there is evidence to support a dose-response relation. Specifically, more frequent work stress [20] and increased reports of work stress in different domains (e.g., demotion, business failure) [18] are associated with an increased risk of CVD. The danger of multiple stressors was also highlighted by Orth-Gomér and Leineweber [24]. They showed that individuals, who were exposed to a combination of work and marital stress, had an increased risk of both a first and recurrent cardiac event compared to individuals who experienced no stress (i.e., risk increased by a factor of ten and six, respectively). Together, these studies show that frequent or chronic stress negatively affects (cardiovascular) health.

It is acknowledged that the negative effect of stress on health occurs in the long run through prolonged physiological stress responses [10, 12, 25]. Yet up until two decades ago, most research focused on how increased physiological activity *during* a stressful situation affected health [26]. Such a *reactivity view of stress* is considered insufficient as it fails to account for *prolonged* physiological activation [26-28]. In recent years, it has become increasingly clear that the stress-disease link may be better explained by stress-related thoughts, like anticipation and rumination. These thoughts keep the stressful event active in one's mind and thereby prolong the stress-related physiological activation [25, 27].

PERSEVERATIVE COGNITION

Even though the majority of research has focused on increased physiological responses

as a result of stressful events, physiological stress responses can also be activated and prolonged by thinking about these stressful events [25, 27-29]. This is particularly important, because the duration of stressful events is usually short compared to the actual amount of time that individuals can think about these events. To explain, completing an exam can be considered stressful for some individuals and this event may last for a few hours. However, individuals may spend days thinking about this event either prior to or afterwards (with thoughts like 'I am going to fail' or 'I am sure I flunked my exam, I am such an idiot'). In addition, individuals may think about future stressful events, but—in reality—those anticipated or imagined stressors often do not occur [30]. For example, you may have worried continuously about getting a negative reaction from your superior after failing to meet a deadline, but in reality your supervisor acted understandingly. By continuously thinking about these (potential) stressful events, the physiological stress response is prolonged and this process is described in the perseverative cognition (PC) hypothesis [25, 31-33]. According to this hypothesis, PC—such as worry—mediates the positive relation between the experience of stressful events and (cardiovascular) health problems by prolonging the exposure to the stressor in ones' mind. In support of this hypothesis, a recent meta-analysis showed that worry was associated with stress-related physiological activity, including low heart rate variability (HRV) [34]. HRV refers to the variability in timing between each heartbeat [35] and low levels of HRV are a known risk factor in the development of CVD [36, 37]. To summarize, stress prolongs stress-related physiological activity by continuously thinking about (potential) stressful events and this can ultimately have negative health effects.

UNCONSCIOUS PERSEVERATIVE COGNITION

In recent years, the PC hypothesis has been extended to include the notion that prolonged physiological stress responses can also be caused by PC that occurs outside an individuals' conscious awareness [38, 39]. This so called 'unconscious stress' is defined as "the ongoing activated cognitive representation of one or more psychological stressors that occurs while conscious attention is directed elsewhere" [38, p. 411]. This idea was put forward since a major part of the prolonged stress-related physiological activity, assessed both in experimental studies and in ambulatory ones, remained unexplained after accounting for relevant biobehavioral and psychological factors [28]. There are several reasons to believe that this unexplained stress-related physiological activity may be due to unconscious stress [28, 38, 39].

The first *indirect* evidence comes from sleep studies. Both laboratory studies [40, 41] and studies in daily life [42-44] have shown that worry and perceived stress

are associated with increased physiological arousal during sleep. Clearly, conscious thought or worry is not possible during sleep. This leads us to believe that stress-related cognitive processes continue in an unattended manner when an individual is asleep and that these unconscious stress-representations affect physiological activity. Even so, roughly one third of the studies found no such effect (see [28]). The second type of evidence comes from a study that was conducted in daily life by Pieper, Brosschot, van der Leeden, and Thayer [32]. They showed that daytime worry increased stress-related physiological activity. Importantly, this effect was still visible 2 hr after the worry episode ended and could not be explained by current worry episodes, or by other psychological or biobehavioral factors. This finding suggests that conscious worry does not sufficiently account for the prolonged stress-related physiological activity. The third type of evidence comes from studies using laboratory stressors. These studies showed that high trait rumination was associated with poorer physiological recovery after the stressor and this could not be fully explained by conscious rumination or worry [45, 46]. Altogether these findings suggest that unconscious stress can affect physiological activity, yet the evidence is indirect and therefore still remains inconclusive.

Direct evidence is however limited, because the majority of stress research has focused on the effect of subjective, self-reported, affective experiences and has largely ignored the importance of unconscious processes for health. Yet it is generally established that affective processes—just like cognitive processes [47]— can occur unconsciously or outside an individuals' awareness [48-52]. Indeed, different experiments have shown that affective reactions can be generated using subliminal stimuli (i.e., stimuli that are presented below the awareness threshold). The induced affective reaction—that occurs independent of explicitly reported feelings—has been found to influence preference for neutral stimuli [53, 54] and behavior [55, 56]. Moreover, subliminal priming paradigms have been shown to influence stress-related cardiovascular activity [57-59]. In a recent systematic review almost half of the summarized evidence was in favor of the idea that unconscious stress can increase physiological activity, with only a fraction of the evidence pointing in the other direction (3%) [60]. This conclusion is, however, limited by the fact that the methodology of the included studies differed significantly from each other and because health-relevant physiological parameters (e.g., HRV, blood pressure) were infrequently addressed. Furthermore, a recent study showed that threatening stimuli shown below the conscious awareness threshold increased total peripheral resistance, but not blood pressure [61]. Even though these findings are promising, there is definitely a need for more studies that specifically address whether unconscious stress can prolong physiological activity in real life.

THE NEXT STEP

The majority of emotional processes is likely to occur outside an individuals' awareness [49, 62] and it is therefore also likely that our minds and bodies are influenced by more than what we can explicitly report. So, in the absence of awareness, unconscious stress-representations may be activated frequently or even continuously and these representations in turn may explain a large part of the prolonged physiological stress-response that ultimately result in deteriorated physical health [38].

In the past years, evidence has been collected that supports the association between PC, or conscious stress-representations, and physiological activity [25, 28, 31-34]. Yet there is only tentative evidence to support the extended PC hypothesis, which hypothesizes that unconscious stress-representations affect stress-related physiological activity. The evidence—as discussed above—is indirect and incomplete. Moreover, research on the (extended) PC hypothesis has mostly been cross-sectional, which limits our conclusions regarding both directionality and causality. In the present thesis, we aim to extent the current findings by manipulating PC (both conscious and unconscious) and simultaneously examining its effect on physiological activity.

One way to test whether (unconscious) PC prolongs physiological activity is to decrease it, because the reverse would be unethical. Specifically, we wish to study the extended PC hypothesis outside of the laboratory, that is, in daily life. Even though a laboratory-based study can provide useful insights, the resulting conclusions may be inaccurate because environmental and contextual factors are not taken into account [63, 64]. The generalizability of laboratory findings to real life was already questioned by Brunswik [65] over 70 years ago and he was a strong advocate for studying individuals in their natural environment. Despite this early advocacy for real life studies, the majority of studies have taken place in the confines of the laboratory [63]. Recent technological developments have, however, made it easier to study individuals in real life (e.g., by using smartphones). By examining the relation between (unconscious) PC and physiological activity in daily life we intend to provide empirical evidence for the extended PC hypothesis that is not confined to the controlled laboratory setting.

Below we discuss two interventions that aim to reduce (unconscious) PC. That is, a worry-reduction intervention and a subliminal evaluative conditioning intervention that reduces automatic negative self-evaluations, which are prevalent under stress. If such interventions succeed in lowering unconscious stress, we can examine whether these changes are associated with reductions in prolonged physiological activity, specifically cardiovascular activity. Such data would provide more direct evidence for the hypothesis that unconscious stress causes prolonged physiological activity.

Worry-Reduction Intervention

Studies are warranted that examine whether reducing worries in daily life also impacts health. For two reasons, it is likely that such worry-reduction interventions will not only reduce the worries themselves, but also unconscious stress. First of all, theoretically a positive association is expected between conscious worry and unconscious stress. To explain, the worries themselves can become more or less automatic and habitual. Thus, if the intervention reduces conscious worries, the associated unconscious stress is also expected to decrease. Second of all, several studies show that skills can become automatized through repetition and thus become unconscious (i.e., no longer requiring awareness) [47, 50]. It is conceivable that a worry-reduction intervention, through frequent repetition, can lead to automatization of the targeted cognitive changes and this will likely reduce unconscious stress. Indeed, a review [66] discussed that mental exercises like cognitive training and meditation can cause cognitive-behavioral changes that are supported by changes in the brain, just as with learning new skills (e.g., playing the piano).

Repetition is suggested to be fundamental for changing habits, such as worries [67, 68]. Even though repetition is relatively hard (and costly) to accomplish using traditional face-to-face therapies, it is more feasible when interventions make use of recent technological developments. Interventions that are for example delivered over the Internet are more easily accessible and the training is not restricted to a specific place and time (e.g., therapist office, 1 hr a week) [69]. This means that users of Internet interventions have more repetition possibilities for the new behavior. Importantly, adherence to Internet interventions is good and these interventions can improve mental health [70].

An even more recent advancement is the use of electronic devices—typically smartphones—to deliver interventions in daily life. These ecological momentary interventions (EMIs) have numerous advantages compared to traditional face-to-face therapies [71-73]. First and foremost, EMIs make it possible to train people when the maladaptive behavior is actually occurring. This is important because when people experience stress they are more likely to revert to their habit behavior (e.g., worry) and they are less likely to implement a newly learned behavior routine [74-76]. As worry is a mental habit that is automatically triggered by (potentially) stressful experiences, it might be particularly important for worry-reduction interventions to target these worries directly when they occur. Second, by training people in daily life (i.e., when the maladaptive behavior occurs), the EMI allows for the formation of a new and more adaptive link between context and behavior. Third, EMIs are cost-effective and can be delivered to anyone, anywhere, as long as that person is in possession of or has

access to a smartphone. Reviews suggest that EMIs can be effectively used to improve mental health [73, 77] (see *Chapter 3* for a full discussion on the effectiveness of EMIs). To sum up, EMIs can be used to train people—repeatedly—throughout their daily lives and specifically in those instances when individuals worry.

Summarizing, Internet interventions as well as EMIs seem suitable to study to what extent reducing worries and unconscious stress in daily life affects physiological activity, as these types of interventions focus on training new skills in the environment where the problems actually occur. Implementing Internet- and smartphone-delivered worry-reduction interventions in daily life will enable us to study the validity of the extended PC hypothesis in an ecologically valid way.

Subliminal Evaluative Conditioning Intervention

Besides studies that focus on reducing conscious worries and the associated unconscious stress, there are also methods to target unconscious stress directly. Specifically, subliminal evaluative conditioning (SEC) [78] can be used to directly target unconscious mental representations of threats to oneself that are prevalent in stressful situations. In this conditioning paradigm the self (using words like 'I' or 'Me') is repeatedly and subliminally coupled with positive affective words. Initial studies suggest that a single session of this procedure can be successfully used to increase implicit self-esteem [78, 79]. Implicit self-esteem is hereby defined as the automatic or unconscious association with the self-concept [80]. To date, no research has examined whether SEC also affects physiological activity, but subliminal priming paradigms have been shown to influence stress-related cardiovascular activity [57-59]. Levy, Hausdorff, Hencke, and Wei [57] for example showed that elderly individuals who were primed with positive age stereotypes had attenuated blood pressure and skin conductance responses during a stressful task. A reverse pattern was observed when individuals were primed using negative age stereotypes. These findings suggest that a subliminal paradigm can affect stress-related physiological activity and it is conceivable that SEC has similar effects (considering the procedural overlap). Thus, SEC may have the potential to change both unconscious mental representations of threats to oneself and stress-related physiological activity. Once we have demonstrated that SEC indeed reduces unconscious stress-representations and stress-related physiological activity in controlled circumstances (i.e., laboratory), the intervention can subsequently be implemented and further examined in daily life. It could potentially be used as a short and cost-effective intervention (i.e., programmed on a smartphone).

AIMS AND OUTLINE

This thesis aims to provide a more complete insight in how stress affects health. Specifically, we aim to test the (extended) PC hypothesis by examining whether interventions designed to reduce conscious worry (*Chapters 2, 4, and 5*) and unconscious stress (*Chapters 4-6*) improve health-related parameters. To reduce worry and unconscious stress, two different strategies are employed. First, we examine whether repeatedly training people in their daily life is effective (*Chapters 2-5*). Second, we study whether unconscious stress can be directly manipulated by targeting automatic negative self-evaluations, which are prevalent under stress (*Chapter 6*). Manipulating these stress-representations will enable us to draw conclusions about causality and directionality.

In *Chapter 2* we test an Internet-based worry-reduction intervention in the general population and examine its effectiveness in reducing conscious worry and subjective health complaints.

In *Chapter 3* we carry out a systematic review and meta-analysis to get an up-to-date and comprehensive overview of the effect of smartphone-based interventions on mental health and positive psychological outcomes.

In *Chapter 4* we discuss the feasibility and preliminary effectiveness of a smartphone-based worry-reduction intervention with mindfulness exercises in high worrying students. The effectiveness of the intervention is further examined in a large-scaled randomized controlled trial in people suffering from work stress in *Chapter 5*. In both chapters we examine whether the intervention led to reductions in both conscious and unconscious stress thereby possibly mediating improvement in ambulatory assessed cardiovascular activity.

In *Chapter 6* we present the results of three different experiments in which we aim to reduce automatic negative self-associations in high worrying students by repeatedly and subliminally coupling the self to positive trait attributes. The effect of this subliminal evaluative conditioning procedure is examined on unconscious stress and cardiovascular activity.

At last, in *Chapter 7* the main findings of the different studies are summarized and discussed. Moreover, the thesis' limitations, implications (both theoretical and clinical), and future directions are presented.

Reducing worry and subjective health complaints: A randomized trial of an internet-delivered worry postponement intervention

02

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ABSTRACT

Objectives

Several studies have shown that perseverative, worrisome thoughts are prospectively related to subjective health complaints (SHC) and that a short worry postponement intervention can decrease these complaints. As SHC and worry are prevalent and costly, we tested whether the intervention can be offered online to reduce these complaints in the general population.

Design

A randomized parallel-group trial was conducted with self-selected participants from the general population.

Methods

Via the research website, 996 participants were instructed to register their worrying for 6 consecutive days. The intervention group was instructed to postpone worry to a special 30-min period in the early evening. The Subjective Health Complaints inventory, as administered before and after the intervention, and daily worry frequency and duration were considered the primary outcomes.

Results

Three hundred and sixty-one participants completed the study. Contrary to our expectation, the registration group (n = 188) did not differ from the intervention group (n = 163) in SHC = .00, CI [0.000,0.003]), or in worry frequency or duration. Nevertheless, the different worry parameters were moderately related to SHC (r between .24 and .34, $p \leq .001$).

Conclusions

In contrast to previous studies using pen-and-pencil versions of the worry postponement intervention, this study suggests that a direct online implementation was not effective in reducing SHC and worry. Overall, participants had high trait worry levels and reported difficulty with postponing worrying. Reducing SHC and worries via the Internet might require more elaborate interventions that better incorporate the advantages of delivering interventions online.

INTRODUCTION

Worry is a common phenomenon and can be defined as a 'chain of thoughts and images, negatively affect-laden and relatively uncontrollable' [81, p. 10]. Although some people believe that worrying has benefits (e.g., problem solving), people generally report the negative sides related to worrying. Several studies have shown that excessive worry is an important aetiological element in different psychopathological conditions, for instance, generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), anxiety, and depressive disorders [81, 82]. Furthermore, worrying has been related to heightened physiological activity, including cardiovascular and endocrinological activity, and dysregulation of immunological activity [25]. This is a concern, given that prolonged physiological activity carries health risks; for example, prolonged heart rate is predictive of coronary heart disease and even cardiovascular death [83]. Several studies found that worry may increase the risk for coronary heart disease [84, 85]. These findings are in line with the perseverative cognition (PC) hypothesis, which suggests that PC, such as worry and rumination, prolongs physiological activation beyond the presence of a direct stressor, and that this prolongation of the stress response may lead to health problems [25]. In other words, according to this hypothesis, PC acts as mediator by which psychosocial stress may produce negative health effects.

A review by Verkuil, Brosschot, Gebhardt, and Thayer [31] supports an association between PC and health. Specifically, most of the reviewed articles found that PC was positively associated with subjective health complaints (SHC) and cardiovascular activity. Moreover, an ambulatory study by Verkuil, Brosschot, Meerman, and Thayer [33] showed that worry acts as a mediator between stress and SHC. However, studies that looked at the causal relationship between PC and SHC are still limited [31]. The studies that have examined this causal relationship did so by manipulating worry using a worry postponement intervention [86-88]. In this intervention, participants are instructed to postpone their daily worries to a special 30-min worry period in the early evening [89]. Research has shown that it can reduce daily worrying [89] and decrease SHC [86-88]. The effectiveness of the procedure is attributed to similar mechanisms that underlie fear extinction [89]. Previously conducted studies using worry postponement were carried out amongst young people (i.e., < 18 years) [86, 88] and people suffering from work-related stress [87]. This study aimed to further investigate the causal relationship between PC and SHC in the general adult population.

Besides testing the causal relation between worrying and SHC, as predicted by the PC hypothesis, finding ways to reduce SHC is of great importance as SHC

are highly common in the general population. SHC are associated with large health care costs [90], with lower levels of health-related quality of life [91], and heightened psychological distress [92]. Given this, it is not only theoretically important to test the PC hypothesis (i.e., does reducing worry lead to a decrease in SHC?), but also important to find simple and cost-effective ways to reduce these SHC.

We therefore attempted to replicate the findings of the worry postponement intervention and tested whether it can reduce worry and SHC in the larger general population. In contrast to the previous studies that delivered this intervention on paper [86-88], the present intervention will be delivered over the Internet. Internet-based interventions are increasingly being used for treating various psychological disorders and health problems, and its use carries several advantages like being easily accessible and cost-effective [69]. A meta-analysis has now shown that Internet interventions can be effective in reducing psychological symptoms and result in good adherence [70]. These results seem promising and make it interesting to study the effects of the intervention online.

Individuals in the present study were randomly allocated to either the worry postponement condition or a control condition, in which individuals were asked to merely register their worry frequency and duration (i.e., identical to the previous studies). It was first investigated whether trait worry and worry in daily life (i.e., worry frequency and duration) were related to SHC. Next, the effects of the online worry postponement intervention on SHC and worry in daily life were examined. In case of positive outcomes, this would confirm the causal relationship between worrying and SHCs and—secondly—would make a simple and easily accessible intervention available for a wider audience. Additionally, the effect of the intervention on positive and negative affects was studied. Affect was included, because this intervention manipulates worrying, and worry intensity has been shown to predict the level of negative affect [33]. If the intervention is capable of reducing worry, it may in turn also decrease the level of negative affect. Furthermore, it is important to confirm earlier findings that effects of worry on SHC are independent of negative affect [88]. Based on earlier findings with the 'regular' offline version of the intervention, it was expected that the online intervention would reduce the number of SHC and the level of daily worrying (both frequency and duration). Furthermore, it was expected that the intervention would lead to a decrease in negative affect.

METHOD

Design

A non-stratified randomized parallel-group trial was conducted with self-selected participants from the general population. The study was conducted between 2005 and 2012 and was not pre-registered. The institutional review board approved the study.

Participants

Dutch participants were recruited to participate in an online study on daily worrying via advertisements in local and national newspapers, and the Internet (e.g., websites of popular magazines). People who were interested in volunteering were directed towards the website of the study http://www.piekeren.com ('piekeren' is the Dutch word for worrying). The website was typically in the top 10 results when the word worrying was entered into a search engine. The website was described as 'Participate in a scientific study on worry and being concerned.' On the website, participants were instructed to attentively read the information about the study. It clarified that the research aimed to compare two different techniques to deal with worrying and that worry registration would be central in both techniques. Everyone was informed that, for 6 days, they would have to use registration forms to record the amount of worrying that occurred during the day. It was explained that registering worrying is easy and helps to provide insight into ones worry behavior. People were asked to complete the whole study, which consisted of (a) completing questionnaires and (b) registering frequency and duration of worry episodes for 6 consecutive days. However, people were informed about their freedom to exit the study at any given point without consequences.

To be included in the study, participants had to be 18 years of age or older. No further exclusion criteria were used. A total of 1,035 people registered on the website, of whom 996 were 18 years of age or older. Of this group, 361 completed the entire study. High dropout rates are commonly seen in online interventions that are open to the entire community [93]. The final population consisted of 55 males and 306 females, with a mean age of 36.36 years (SD = 12.97).

Questionnaires

Penn state worry questionnaire. This 16-item self-report measure assesses trait worry; specifically, it measures the tendency, intensity, and uncontrollability of pathological worry [94, 95]. It is a psychometrically sound instrument, with high internal consistency, good test-retest reliability, and good predictive validity [94-96]. Internal consistency (Cronbach's $\alpha = .89$) was high in the present study. This questionnaire was

administered before the start of the worry registration.

Subjective health complaints inventory. This inventory makes it possible to easily and reliably measure the amount of SHC during the last 30 days in the general population using 29 items [97]. For each of the 29 complaints, participants have to rate the severity and the number of days that the health problems were troubling them. Instead of asking about complaints during the past 30 days, we asked about the presence of these problems during the past three days. Moreover, in line with Verkuil et al. [33], two items regarding anxiety and depression were removed, because these do not represent *physical* complaints. As in the previous studies, the total number of complaints was used as outcome variable in this study. The internal consistency was good at pre- and post-intervention (both Cronbach's α of .83).

Positive and negative affect schedule. The Positive and Negative Affect Schedule (PANAS) is a valid and reliable measure of positive and negative affect in both clinical and non-clinical populations [98, 99]. Participants have to score the extent to which they experience the different emotions (e.g., interested, afraid) using a 5-point scale, ranging from 'very slightly' to 'very much.' The time frame that was used was 'in general' before the worry registration (T1) and 'during the past 6 days' after the worry registration (T2). Internal consistency, as measured by Cronbach's alpha, was considered high for both positive and negative affects at both T1 (.88 and .88, respectively) and T2 (.89 and .89, respectively).

Worry log. Whenever participants were worrying, they were instructed to note this down on a form that participants had to download from the website (see Appendix 1). At the end of each day and each morning, participants estimated the total number of worry episodes (i.e., worry frequency) and duration of these episodes. Participants had to follow these instructions for 6 consecutive days. The form has previously been used by Brosschot and van der Doef [88] and Verkuil et al. [96].

Worry Postponement Intervention

On the back of the worry log, participants in the worry postponement condition received additional instructions. They were instructed that every time they noticed they were worrying, they had to try to postpone this worrying to a special 30-min worry period at the end of the day. The same procedure has been used by Brosschot and van der Doef [88]. The following specific instruction was used:

> A frequently used method to deal with worrying is to set a special half-an-hour worry period. It works like this, every time you realize that you are worrying, you need to try to stop worrying and postpone the worrying to a moment later

on in the day (i.e., the half-an-hour worry period). We ask you to start with this tomorrow and continue with the half-an-hour worry period for 6 consecutive days. [88, p. 23]

Procedure

After people registered on the site using their email address, the computer employed a simple randomization scheme to allocate participants to either the experimental or control condition. After login, all participants had to fill in several demographic questions (i.e., age, gender, level of education, type of job, living situation, duration of sporting activity, amount of weekly alcohol intake, number of cigarettes weekly smoked, and sleep quality and duration), complete three measures (Penn State Worry Questionnaire [PSWQ], SHC, and PANAS), and read about how to register their worrying. In addition, participants in the experimental condition were told to postpone their worrying to a special 30-min period in the early evening. The registration (or registration and intervention) period started the day after participants had completed the questionnaires and lasted 6 days and nights. To register worrying, participants had to print the worry log and use this for daily worry registration. Next, worry frequency and duration had to be registered online; this could be carried out daily or at the end of the registration period. Participants received daily emails to remind them of their worry registration. After the 6 days, participants filled in a second SHC, PANAS, and two questions about their sleep quality. Additionally, after completing the intervention, adherence to the registration was checked with the question 'To what extent did you succeed in registering the worrying?' Participants in the intervention group also rated how successful they had been at postponing worrying during the intervention period (i.e., 'To what extent did you succeed in postponing the worrying to the special 30-min worry period'). Both questions were rated on a 10-point scale, ranging from 'very bad' to 'very good.' Participants were then acknowledged for their participation. The entire procedure operated independently of the researchers.

Statistical Analysis

A Pearson partial correlation was used to assess the relation between trait worry and SHC at T1, controlling for negative affect at T1. To examine whether daily worry frequency and duration on the first three days was related to SHC at T2, additional Pearson correlations were performed in the control condition (i.e., amongst participants who had not been influenced by the worry postponement) [88]. To assess whether the intervention had an effect on SHC and affect, a repeated-measures ANOVA was performed with the timing of the measurement (i.e., T1 or T2) as the within-subject

variable and condition (i.e., control or experimental condition) as the between-subject variable.

To determine whether changes in worrying during the 6 days were related to condition or to changes in SHC, linear bootstrap regression analyses were carried out. In contrast to traditional regression analyses that involve a dependent variable with a single level, in linear bootstrap regression analyses, a dependent variable can consist of repeated measures (i.e., of worrying). Because the worry data consists of repeated measures, dependency amongst the measures exists and this dependency can bias the resulting standard errors. Unbiased standard errors can be obtained using a bootstrap procedure [100, 101]. This particular procedure was chosen, because this analysis was capable of handling the non-normal responses [102]. It is a procedure in which new samples of the same sample size as the original sample are formed with replacement. The variation in estimated parameters across the newly created samples is used to get an unbiased standard error [102]. To study the condition effect, bootstrap regression models were built for both worry frequency and duration including the predictor time, condition, and the interaction between these two predictors. The Time X Condition interaction was our main focus, because it shows whether the intervention was capable of reducing daily worry over time. Bootstrap regression models were also used to examine whether changes in worry were related to changes in SHC whilst controlling for changes in negative affect. Here, the interaction between time and change in SHC was our main interest, as it shows whether changes in worrying over time are related to changes in SHC. This analysis was conducted using data from the control condition only, as the worry data of this group was not influenced by the worry postponement intervention (cf. [88]).

Linear regression with bootstrap was performed using RStudio (version 0.98). The other analyses were conducted using the Statistical Package for Social Sciences, version 21.0 (IBM Corp., 2012).

RESULTS

Descriptive Statistics

Figure 1 shows the flow chart of participants. Of the participants that registered on the website, 508 stopped during or after filling in the baseline questionnaires and 127 stopped during the intervention period, resulting in a total of 361 participants who completed the entire study. Due to a programming error, only a subsample of the participants (n = 317) received a PANAS measure at T2. Ten participants were excluded from the analyses on the basis of three different criteria. Six participants were

excluded because the number of reported worry episodes was far greater than the total duration of those episodes in minutes. To illustrate this, one participant reported a total of 240 worry episodes in one day, with total worry duration of 30 min. As these figures seem highly unlikely, participants with similar data were excluded. Two more participants were excluded, because the duration of their daily worrying was extreme, namely 840 min (i.e., 14 hr) or higher. Lastly, two participants were excluded, because the duration of nightly worrying exceeded 360 min (i.e., 6 hr). This resulted in a final sample size of 351.

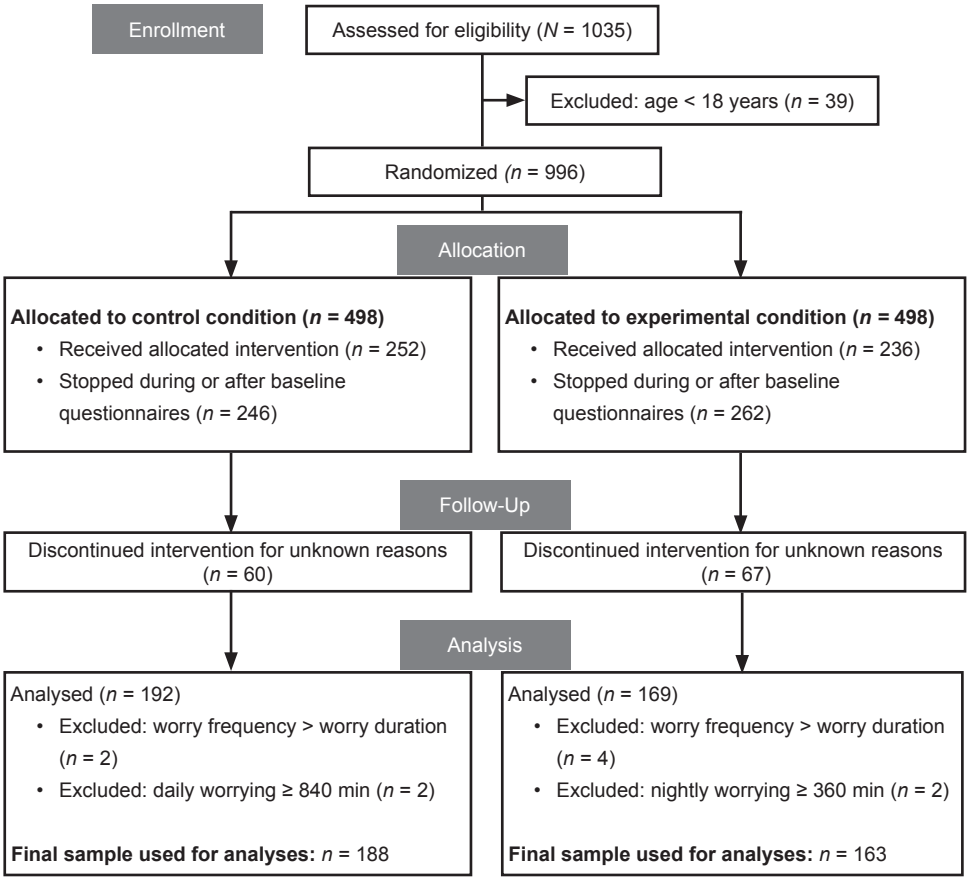

FIGURE 1 Flow diagram of participants during this trial

Table 1 displays the descriptive statistics of both the final population and of the participants who dropped out (i.e., participants who did not finish the study and participants who

were excluded). Dropout was not related to condition, with $\chi^2(1, 996) = 2.75$, $p = .097$. The dropout participants were significantly younger than the participants who finished the intervention, with $t(666.31) = -2.65$, $p = .008$. In addition, a chi-square test revealed that males were more likely to drop out compared to females, $\chi^2(1, 996) = 4.34$, $p = .037$, $\phi = .07$. Moreover, the final population had lower levels of trait worry and negative affect, and higher levels of positive affect compared to the dropout group, $t(994) = 2.12$, $p = .035$, $t(994) = 4.89$, $p < .001$, and $t(994) = -3.28$, $p = .001$, respectively. Lastly, no significant differences were found between the two groups on SHC, with $t(994) = 1.70$, $p = .090$; or the level of education, with $\chi^2(1, 996) = 1.31$, $p = .726$.

TABLE 1 Descriptive statistics of the final population and dropout participants at baseline

	Final population (n = 351)			Dropout participants (n = 645)		
Variable	%	Mean	SD	%	Mean	SD
Gender	85% female			80% female		
Age		36.23	12.96		34.02	11.86
PSWQ		56.72	11.38		58.27	10.75
SHC		9.32	4.53		9.88	4.67
NA		23.66	8.03		26.51	8.48
PA		31.32	7.83		29.41	7.80
Registration		6.73	1.69		—	—

Note. NA= negative affect subscale of the Positive and Negative Affect Schedule; PA= positive affect subscale of the Positive and Negative Affect Schedule; PSWQ= Penn State Worry Questionnaire; Registration = the extent to which participants succeeded in registering worrying; SHC= Subjective Health Complaints inventory.

The final sample consisted of 52 men and 299 women, with a mean age of 36.23 years (SD = 12.96). The experimental condition consisted of 163 participants and the control condition of 188. There were no differences between the conditions on any of the descriptive variables. The average trait worry score as measured by the PSWQ was 56.72. Female participants scored significantly higher on trait worry compared to male participants, respectively, 57.78 (SD = 10.45) and 50.67 (SD = 14.38) with $t(60.71) = -3.41$, $p = .001$. Men and women did not differ significantly on the other descriptive variables. The average level of adherence to the registration was 6.73 (SD = 1.80; NB. on a 10-point scale, ranging from ‘very bad’ to ‘very good’) for all participants and those in the experimental group scored their ability to postpone their worrying on average 4.09 (SD = 2.53; idem). The mean number of worry episodes that participants in the control condition reported per day was 6.98 (SD = 6.30), and the mean duration of these episodes per day was 76.66 (SD = 80.66). In the final sample, the timescale in which participants finished their intervention varied highly (i.e., from 2005 to 2012).

However, the year of completion did not significantly differ between conditions with $t(349) = 1.10$, $p = .271$. There were significant positive but small correlations between year of completion and SHC and trait worry at T1, $r(351) = .20$, $p < .001$ and $r(351) = .26$, $p < .001$, respectively, but not with total worry frequency and total worry duration.

Relation between Worry and Subjective Health Complaints

There was a moderate positive correlation between trait worry and SHC at T1 with $r(349) = .34$, $p < .001$. Yet this correlation was no longer significant when controlling for negative affect at T1, $r(345) = .04$, $p = .453$. Furthermore, in the control condition there was a moderate positive correlation between worry frequency on the first three registration days and SHC at T2, $r(184) = .31$, $p < .001$. Likewise, a correlation was found between worry duration on the first three registration days and SHC at T2, $r(184) = .24$, $p = .001$. However, change in SHC was not related to change in worrying when controlling for change in negative affect, as indicated by the non-significant Time X SHC-change interaction of the bootstrap regression models for frequency (B = -0.02, CI [-0.06, 0.03]) and duration (B = -0.23, CI [-1.04, 0.57]), indicating that daily worry was prospectively related to SHC, but not related to changes in SHC.

TABLE 2 Mean (and SD) of SHC, NA, and PC at T1 and T2 for the experimental and the control condition

Variable	Time	Experimental condition	Control condition
SHC	T1	9.28 (4.72)	9.35 (4.38)
	T2	8.48 (4.76)	8.52 (4.12)
NA	T1	24.79 (8.16)	24.14 (7.90)
	T2	23.67 (8.53)	23.64 (8.15)
PA	T1	30.67 (8.45)	31.16 (7.63)
	T2	29.04 (7.94)	29.26 (7.42)

Note. NA= negative affect subscale of the Positive and Negative Affect Schedule; PA= positive affect subscale of the Positive and Negative Affect Schedule; SHC= Subjective Health Complaints inventory.

Effect of Worry Postponement on Subjective Health Complaints and Affect

Repeated measure analyses were performed to examine whether SHC, negative affect, and positive affect changed from baseline (T1) to post-intervention (T2) as a result of the intervention.

Subjective health complaints. There was a significant decrease in SHC from T1 to T2 with $F(1, 347) = 31.62$, $p < .001$, $\eta_p^2 = .08$, CI (0.04, 0.14). However, contrary to our expectation there was no difference between the two conditions, $F(1, 347) = -0.02$, $p = .885$, $\eta_p^2 = .00$, CI (0.000, 0.003). Descriptives of SHC are displayed in Table 2.

Affect. Furthermore, negative affect also significantly decreased from T1 to T2, $F(1, 306) = 4.66$, $p = .032$, $\eta_p^2 = .02$, CI (0.00, 0.05). Contrary to our hypothesis, no significant difference in this decrease in negative affect was found between the two conditions, $F(1, 306) = 0.70$, $p = .405$, $\eta_p^2 = .002$, CI (0.00, 0.03). A similar pattern was found for positive affect. Thus, a significant decrease in positive affect over time was found, $F(1, 306) = 18.34$, $p < .001$, $\eta_p^2 = .06$, CI (0.02, 0.11), and this change was not significantly different between the conditions, $F(1, 306) = 0.11$, $p = .739$, CI (0.00, 0.02). Descriptives of negative and positive affects are shown in Table 2.

Effect of Worry Postponement on Daily Worry Frequency and Duration

To determine whether the online worry postponement intervention lowered worrying over time in daily life (both frequency and duration), linear regression analyses with clustered bootstrapping of the standard errors were conducted. The results of the regression models are depicted in Table 3. Furthermore, Figures 2 and 3 display the mean number of worry episodes and the mean duration of those episodes per day for the two conditions.

Worry frequency. The main effect of time was significant, indicating an overall decline in the number of worry episodes over time, B = -0.31, CI (-0.46, -0.15). However, contrary to our expectation, the Time X Condition interaction was not significant (B = 0.20, CI [-0.03, 0.43]), implying that the average change trajectory for worry frequency was not different for the two conditions. Furthermore, the main effect of condition was also significant, B = -1.68, CI (-3.08, -0.28; see Figure 2). Specifically, individuals in the experimental group reported, on average, less worry episodes during the 6 days, compared to individuals in the control condition (respectively, 6.27 and 7.75 episodes on day 1). The overall model was fit with an $R^2 = .01$. To examine whether the effect of condition on the frequency of worry episodes was dependent on the presence of the nonsignificant interaction effect in the model, the interaction term was removed. Results showed that the effect of condition was no longer significant, with B = 0.98, CI (-2.17, 0.20).

Worry duration. For worry duration, neither time, nor condition, nor the interaction between time and condition significantly predicted worry duration (respectively, B = -2.44, CI [-5.52, 0.64], B = -10.67, CI [-33.87, 12.52], and B = 0.58, CI [-3.22, 4.39]), indicating that the average change trajectory of worry duration had a slope of zero, that there was no difference in the average worry duration between the conditions, and most importantly, that the average change trajectory for worry duration was not different for the two conditions. The explained variance of the overall fitted model was $R^2 = .003$.

TABLE 3 Results of the bootstrap regression models predicting the frequency and duration of worry (n = 351)

Model	R^2	B	SE B	d	95% CI LL	95% CI UL
Worry frequency	.01					
Constant		8.06	0.55		6.97	9.14
Time		-0.31*	0.08	-0.12	-0.46	-0.15
Condition		-1.68*	0.71	-0.14	-3.08	-0.28
Time x Condition		0.20	0.12	0.05	-0.03	0.43
Worry duration	.003					
Constant		85.20	8.33		68.87	101.54
Time		-2.44	1.57	-0.06	-5.52	0.64
Condition		-10.67	11.83	-0.05	-33.87	12.52
Time x Condition		0.58	1.94	0.01	-3.22	4.39

Note. B = coefficient; CI = confidence interval; d = standardized mean-difference effect size; LL = lower limit; SE B = bootstrap standard error of the coefficient; UL = upper limit.
* = $p < .05$.

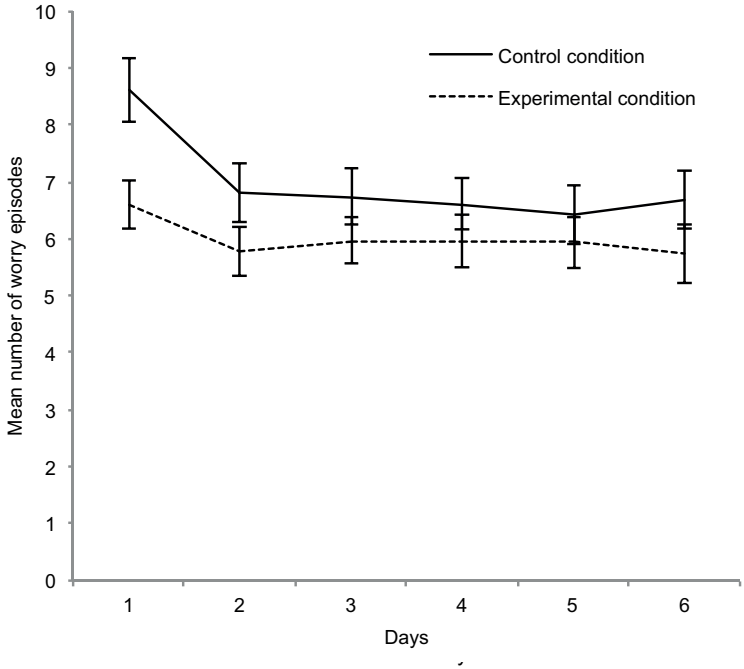

FIGURE 2 Line graph representing the mean frequency of worry episodes over time per condition. Error bars represent ± 2 SE.

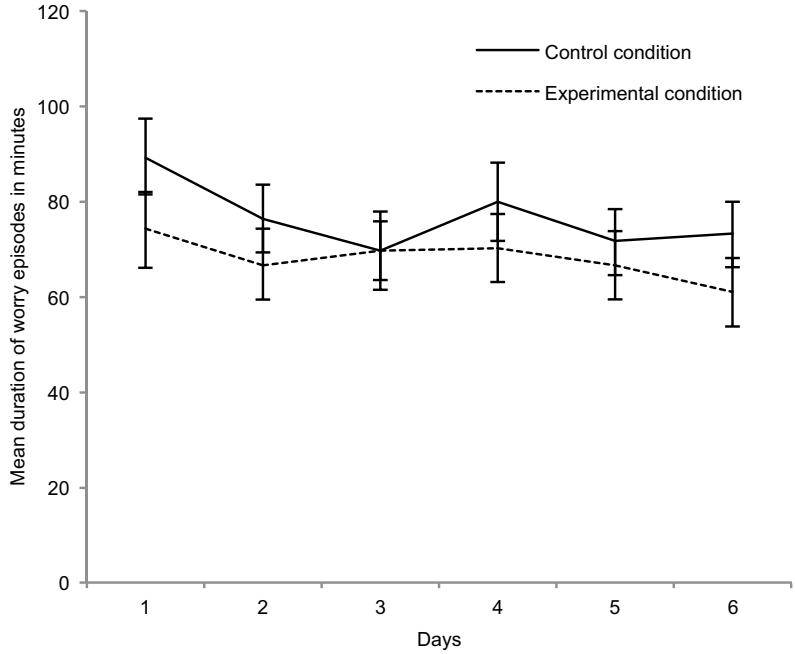

FIGURE 3 Line graph representing the mean duration of worry episodes in minutes over time per condition. Error bars represent ± 2 SE.

DISCUSSION

The current study was conducted to examine the association between worry and SHC, and to test the effectiveness of a worry postponement intervention in reducing SHC, daily worry, and negative affect. Findings indicated that trait worry was positively associated with SHC at baseline; however, daily worry was not associated with changes in SHC. Moreover, a decrease was found in SHC, negative affect, and positive affect. However, contrary to our expectation, participants who received the intervention did not demonstrate a greater reduction in the number of SHC, compared to participants who merely registered their worries. In addition, no robust significant differences between conditions were found in daily worry, negative affect, and positive affect. In short, the main finding is that no evidence was found that the worry postponement intervention reduced the number of SHC as was previously found [86, 88].

We did find that all participants showed a decrease over time in SHC, negative affect, and positive affect. Although it could be argued that merely registering worries had a beneficial effect on SHC and negative affect, the decrease in these complaints was small and a reduction in positive affect was also found which is inconsistent with

a beneficial effect of registering. Therefore, the overall decline in these scores remains somewhat puzzling, but could be explained using the literature on measurement reactivity [103]. That is, it has been repeatedly found that when people are asked to fill in questionnaires about emotions at two occasions, a decline in emotions is found from pre- to post-intervention.

With the current findings, no unequivocal conclusion can be drawn regarding the PC hypothesis, which hypothesizes that PC or worry influences SHC and acts as a mediator between stress and SHC and other health indicators [25, 31]. Given that the worry postponement intervention did not cause a change in worrying over time, we were not able to test this fundamental assumption of the PC hypothesis. However, we did replicate the finding that trait and daily worry were moderately associated with SHC, with high worriers reporting more SHC [31, 88]

A couple of explanations can be offered for why no effect of worry postponement was found [88]. First of all, the difference could be due to the characteristics of the sample, which had relatively high levels of trait and daily worrying. Specifically, the average trait worry was above a cut-off score that is used to screen for GAD [104] and the average daily worrying was fairly high when compared to other non-clinical samples [33, 96]. It is possible that for people with enhanced levels of worry, the postponement intervention was too simple, too brief, or both in its current format. However, this seems unlikely, given that the intervention has been successfully implemented in individuals experiencing work stress [87].

A second explanation for the null results pertains to the procedure that was used. In addition to the registration and postponement instructions (which were similar to the previous studies), participants were now also asked to record their worry frequency and duration online, and daily reminders were send that participants were required to do so. This additional procedural demand could have increased two kinds of worries: (a) worries about partaking in the study and (b) these daily reminders could have served as a reminder about their other worries. Still, it seems unlikely that these procedural changes could account for the null findings. That is, reminders were sent to people in both conditions, and the hypothesized increase in worry would have been observed in both groups.

There are also reasons to assume that the paper-and-pencil design that was used in previous studies cannot be readily translated into an online format. In this study, we choose to replicate the findings obtained with a simple and short worry intervention, with little additional information about the intervention, and for example, about the need to practice it daily. It is possible that the intervention will be effective when delivered online, but maybe only when certain transformations are incorporated

into the design. Indeed, Ritterband et al. [105] stated that actions need to be taken when changing an intervention to an Internet format. These actions, for example, highlight the importance of using multimedia elements (e.g., video or audio) to make the intervention more appealing, to use strategies to personalize the intervention to the individual, and to provide feedback during the intervention. However, in this study these strategies were not incorporated—because the aim was to replicate previous findings with this simple and short intervention—which could explain why the worry postponement did not result in a significant decrease in worries. Moreover, an online format is considered non-committal and more informal for participants. This may lead to a less active participation and ultimately result in a diminished effect. In the future, instead of delivering the intervention via the Internet, it might be worthwhile to use smartphones, as this offer the potential to collect a large amount of ecological valid data in an easy and unobtrusive way, thereby ensuring commitment [71, 106].

The null findings could also be explained by the difficulty in postponing worries. After the intervention, participants rated their ability to postpone worrying quite low (i.e., 4.1 on a 10-point scale); only 39 individuals scored their success a six or higher. So, although individuals were able to register their worrying (i.e., scoring a 6.7), they were less able to postpone worrying to a later moment. In other words, it is possible that worry postponement was too difficult to master in 6 days, at least for this group. Unfortunately, no comparable data from previous studies was available. Also, the ability to register and postpone worrying was only measured once; however, it is conceivable that the fidelity with the intervention fluctuates over different days. Future studies are recommended to daily assess whether participants practiced with the intervention. Moreover, studies might focus on strategies that could improve the applicability of the worry postponement intervention. One option would be to send daily emails to participants to remind them that they should postpone their worrying (instead of only reminding them about the worry registration as done in the current study). An even better option would be to send multiple

reminders during the day (e.g., using smartphones). This repetition may help to increase the automaticity of the target behavior, that is, postponing worrying [67].

Several other limitations need to be discussed, foremost the high dropout percentage (i.e., 64%). Specifically, individuals with high levels of complaints were more likely to drop out. This is in line with a review by Davis and Addis [107],who showed that people with high levels of emotional distress are quicker to drop out. Although the reason for their dropout is unknown, it may be that these individuals are quicker to label an intervention as taxing and thus drop out. High dropout tends to make research less credible; however, high dropout rates are commonly seen in Internet

interventions, especially when online interventions are open to the entire community [93, 108]. Eysenbach [108] suggests making a distinction between initial dropouts/ nonusers and trial dropouts. Using this criterion, the dropout percentage declines to 26%, which is considerably less dramatic compared to 64%. Nevertheless, it would be interesting to determine which predictors determine dropout rate (e.g., duration of intervention, disease severity), in order to learn how interventions can best be used to help individuals.

A second limitation is the overrepresentation of women in this study, but this is not unusual as women are known to have a higher worry level than men [109]. Considering that there are no differences in the gender distribution across conditions, gender could not bias the findings. Lastly, the duration of data collection was 4 years, which means that the participants could have been exposed to different kinds of worries caused by, for instance, the changes in the economy. It could be that some worries are harder to postpone than others. Yet, no empirical study has addressed this. Furthermore, a small to moderate positive correlation between the year of completing the study and trait worry was found. In other words, those who completed the study at a later point had higher trait worry levels. However, year of completing the study did not differ significantly between the conditions and cannot explain the current null findings. The long time frame of the study and the fact that participants started on different days of the week with the intervention can actually be considered as positive characteristics of the study. That is, an intervention aimed at worrying should be effective in reducing this detrimental style of coping with stressful situations, regardless of— for instance— the economic stressors that the participant is experiencing. By conducting a large long-running randomized controlled trial, whereby these factors are assumed to be randomly distributed between conditions, it is possible to study the effectiveness of an intervention under several global circumstances.

As the current results do not support a large-scale online implementation of this particular worry intervention in the general population, alternative ways to reduce worries and SHC are still warranted. Currently, a few other promising strategies have been tested. One of these interventions is expressive writing, in which participants are instructed to regularly write about emotional events. A review, including 146 studies, established that this has a positive effect on both psychological and physiological functioning [110]. The narrative that is formed in expressive writing is argued to help organize complex emotional experiences and this in turn decreases PC [111]. Recent studies investigating expressive writing have indeed shown that it can reduce worry, especially in high worrying individuals [112, 113]. Another promising
intervention is mindfulness-based techniques, in which mindfulness can be defined as

a present focused awareness [114]. Mindfulness has been shown to reduce psychological stress in clinical populations [115] and to reduce stress, ruminative thinking, and trait anxiety in healthy people [116, 117].

To conclude, no evidence was found for the effectiveness of the online version of the worry postponement intervention to lower SHC in the general population. Compared to merely registering worries, no beneficial effects of the postponement intervention were observed in terms of a decline in SHC, negative affect, nor the frequency and duration of worrying. All in all, the online worry postponement instruction cannot be recommended as an effective preventive intervention in the general population to decrease SHC. Considering the burden of SHC, it remains important to find effective interventions that can be easily administered in the general population.

APPENDIX 1 Worry registration form

Fill in during day: Fill in during the evening:

Number of worry episodes (one tally for every episode)

Day 1:

(if none, register: 0) .....

(if none, register: 0) ..... min

Nightly worrying? *Estimate* number ..... (if none, register: 0), and duration .....

Day 2:

(if none, register: 0) .....

(if none, register: 0) ..... min

Nightly worrying? *Estimate* number ..... (if none, register: 0), and duration .....

Day 3:

(if none, register: 0) .....

(if none, register: 0) ..... min

Nightly worrying? *Estimate* number ..... (if none, register: 0), and duration .....

Day 4:

(if none, register: 0) .....

(if none, register: 0) ..... min

Nightly worrying? *Estimate* number ..... (if none, register: 0), and duration .....

Day 5:

(if none, register: 0) .....

(if none, register: 0) ..... min

Nightly worrying? *Estimate* number ..... (if none, register: 0), and duration .....

Day 6:

(if none, register: 0) .....

(if none, register: 0) ..... min

Nightly worrying? *Estimate* number ..... (if none, register: 0), and duration .....

Changing mental health and positive psychological well-being using ecological momentary interventions: A systematic review and meta-analysis

03

Versluis A, Verkuil B, Spinhoven P, van der Ploeg MM, Brosschot JF.
Journal of Medical Internet Research. 2016;18(6):e152.

ABSTRACT

Background

Mental health problems are highly prevalent, and there is need for the self-management of (mental) health. Ecological momentary interventions (EMIs) can be used to deliver interventions in the daily life of individuals using mobile devices.

Objectives

The aim of this study was to systematically assess and meta-analyze the effect of EMI on three highly prevalent mental health outcomes (anxiety, depression, and perceived stress) and positive psychological outcomes (e.g., acceptance).

Methods

PsycINFO and Web of Science were searched for relevant publications, and the last search was done in September 2015. Three concepts were used to find publications: (a) mental health, (b) mobile phones, and (c) interventions. A total of 33 studies (using either a within- or between-subject design) including 43 samples that received an EMI were identified (n = 1301), and relevant study characteristics were coded using a standardized form. Quality assessment was done with the Cochrane Collaboration tool.

Results

Most of the EMIs focused on a clinical sample, used an active intervention (that offered exercises), and in over half of the studies, additional support by a mental health professional (MHP) was given. The EMI lasted on average 7.48 weeks (SD = 6.46), with 2.80 training sessions per day (SD = 2.12) and 108.25 total training sessions (SD = 123.00). Overall, 27 studies were included in the meta-analysis, and after removing 6 outliers, a medium effect was found on mental health in the within-subject analyses (n = 1008), with g = 0.57 and 95% CI (0.45, 0.70). This effect did not differ as function of outcome type (i.e., anxiety, depression, perceived stress, acceptance, relaxation, and quality of life). The only moderator for which the effect varied significantly was additional support by an MHP (MHP-supported EMI, g = 0.73, 95% CI [0.57, 0.88]; stand-alone EMI, g = 0.45, 95% CI [0.22, 0.69]; stand-alone EMI with access to care as usual, g = 0.38, 95% CI [0.11, 0.64]). In the between-subject studies, 13 studies were included, and a small to medium effect was found (g = 0.40, 95% CI [0.22, 0.57]). Yet, these between-subject analyses were at risk for publication bias and were not suited for moderator analyses. Furthermore, the overall quality of the studies was relatively low.

Conclusions

Results showed that there was a small to medium effect of EMIs on mental health and positive psychological well-being and that the effect was not different between outcome types. Moreover, the effect was larger with additional support by an MHP. Future randomized controlled trials are needed to further strengthen the results and to determine potential moderator variables. Overall, EMIs offer great potential for providing easy and cost-effective interventions to improve mental health and increase positive psychological well-being.

INTRODUCTION

One in every three individuals worldwide will be affected by one or more mental health problems during their lives [118]. Yet, only a small portion of those individuals is receiving help for their problems (with numbers varying from 7% to 25% in industrialized countries) [119, 120]. To help those in need, new strategies for enhancing access to and quality of care are needed, and this is recognized in a new policy of the World Health Organization [121]. This newly introduced policy requests methods to increase self-management or self-care of health by, for instance, using electronic and mobile devices. In line with this, Wanless [122] argues that health care productivity can be increased using self-care and that this can have cost-effective benefits. All in all, there appears to be a future for the self-management of (mental) health.

One method that can be used to enhance health self-management is ecological momentary interventions (EMIs) [71]. The key to these interventions is that they can be tailored to the individual and be implemented in real time (i.e., daily life). Mobile or electronic devices can be used to provide these interventions in the daily lives of individuals. With a Web-based survey, Proudfoot et al. [123] showed that 76% of the general population is interested in using mobile technology for either self-monitoring or self-management of health (i.e., if the service was free). Using EMIs has numerous advantages such as the ability to reach large populations at lower costs [124, 125].

Training people in situ could be highly relevant for learning new, healthy behaviors, considering that people under stress typically switch from *goal-directed behavior* to *habit behavior* [74-76, 126]. In other words, when a person experiences stress, that person is more likely to rely on the 'old' behavior routine than display the newly learned behavior routine. In line with this, it might make more sense to learn a new behavioral routine in daily life compared with an artificial surrounding (e.g., the therapist's office) that generally does not resemble daily life. Indeed, research shows that although new behaviors can be effectively learned in artificial surroundings, this knowledge does not always generalize to real-life settings [127]. According to Neal, Wood, and Quinn [68], this is understandable, given that the association between context and the maladaptive behavior may still be in place after traditional treatment. As a consequence, the context (e.g., setting or time of day) can still trigger the maladaptive behavior. Therefore, EMIs may provide a more effective way to train people in daily life than conventional treatment, by training people in the very context in which the maladaptive behavior occurs. As a result, this could lead to the (faster) formation of a new and more adaptive association between context and behavior.

Given that the number of worldwide mobile phone users is immense and

continues to expand [128], it is not surprising that EMI is considered to be the future for therapeutic interventions [129]. Numerous authors highlight that EMI is a relatively new research field, and that the field is constantly evolving due to improvements in mobile technology [63, 73, 129]. It is therefore important to know the current state of affairs in this field. Current reviews suggest that EMIs can be effective, but these reviews are limited for different reasons. First, some reviews focus on a specific intervention [130] or on a specific target population [131]. Second, their sole or main focus is the effect of EMIs on health behaviors (e.g., physical activity, smoking cessation, diabetes management) and not mental health [63, 132, 133]. Third, the current reviews are outdated, especially considering the developmental pace of EMIs (e.g., [73]). A more recent review has been conducted by Donker et al. [77]; however, it included only studies that investigated directly downloadable apps. This substantially limited the number of included studies (n = 8). Fourth, the effect of EMIs on positive psychological well-being (e.g., relaxation, acceptance) has not yet been reviewed, although these outcome types have been included as dependent variables in previous studies [134, 135]. Considering that a person's well-being is not equal to the absence of disease and is associated with increased positive cognitions and even physical health, it is important to also study these positive experiences [136]. To conclude, an up-to-date comprehensive overview or a meta-analysis of the effect of EMIs on mental health, including positive health outcomes, is missing.

This systematic review and meta-analysis therefore attempts to expand the current knowledge by including both mental health outcomes (i.e., perceived stress, anxiety, or depressive symptoms) and positive psychological outcomes (e.g., positive affect or acceptance). For this quantitative analysis, randomization and the presence of a control group were optional. Although the absence of randomization and the lack of a control group may weaken the design and thus the ensuing conclusions, these criteria are necessary to ensure that the presented overview of EMI studies is complete. This is considered critical because an extensive overview is currently lacking. It should be noted that study design was used in the moderator analyses.

Considering that the access to care needs improvement and EMIs can be used for this, it is important to investigate for whom these technologies can be appropriate and what EMI characteristics are associated with increased effects. Therefore, potentially promising moderators of effect size were investigated. Specifically, sample, type of training, how the training was triggered (i.e., automatically or on-demand), support of mental health professional (MHP), and dosage were included because these can be considered key intervention components [137]. Including moderators allows us, for example, to investigate whether an EMI in its own right is effective or whether additional

support by an MHP is necessary to accomplish change. In addition, the design of the study, sample size, and the quality of the study were studied to determine whether the effect size varied as a function of study characteristics. In short, we examined whether mobile technology provides an effective platform for mental health interventions and under which circumstances.

METHOD

The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines were followed [138].

Search Strategies

To find relevant publications concerning EMIs that target mental health, a database search was conducted in both PsycINFO and Web of Science (Core Collection). The search strings that were used consisted of three groups of words, namely words related to: (a) mental health, (b) mobile phones, and (c) interventions. See Appendix 1 for the complete search strings. In both databases, the search was limited to English publications that were peer reviewed. The search strategy was not restricted based on publication year as we aimed to provide a comprehensive overview of how mobile technology can be used to improve mental health. Naturally, the technologies that are used in more recent publications may be more advanced compared with earlier publications, but the idea of repeatedly training people in their daily lives is equal in older and newer publications. The last search was conducted on September 17, 2015. In addition, two other search strategies were used. First, the reference lists of previous reviews in the field of EMI were screened for relevant publications. Second, the reference lists of our primary selected papers were examined.

To ensure that no relevant publications were missed with the aforementioned search strategies, an extra search with a similar search string was conducted in the PubMed database on November 2, 2015. This resulted in 3505 publications, and the first 10% was screened to determine whether potentially relevant studies had been missed. However, no relevant publications—that had not already been identified in the other databases—were found, indicating that the used search strategies were sufficient.

Study Selection

Titles and abstracts of publications were first screened for eligibility, and if insufficient information was described in the abstract, the full-text papers were obtained. When a full-text paper was not available, a request was sent to the authors. A number of

inclusion criteria were used for both within- and between-subject studies, which were established by authors AV, BV, and JB. First, publications were included when an EMI was studied (e.g., via smartphone or personal digital assistant)—either as a stand-alone intervention or in combination with other treatment components. Second, the EMI should be automated and operated independently from a therapist. Thus, studies were excluded when the therapist administered the therapy—for instance—via mobile phone or conference call. This criterion was chosen because of our interest in how new technologies could be used to deliver *cost-effective* treatments in daily life, which precluded those requiring comparatively conventional therapist's efforts. Third, a mental health-related outcome should be targeted (e.g., anxiety, depression, or positive psychological well-being and not a health-related outcome such as physical activity). Fourth, the EMI should be studied in an ambulatory setting and not in standard therapy sessions. Publications were excluded if a mental health-related outcome was included, but the training was not directly focused on improving mental health (e.g., psychoeducation for health behaviors or hypertension management). Moreover, studies that did not discuss post-intervention outcome data, without a baseline measure, methodological papers, case studies, reviews, non-peer-reviewed papers, and non-English papers were excluded. Three publications were additionally excluded because the samples were already discussed in other, already included publications. If a study included a control group—in addition to the group that received the EMI—it was coded as a between-subject study (see *Coding* for further details). The screening was conducted by author AV, and uncertainty about the potential inclusion or exclusion of a paper was resolved with authors BV and JB.

Coding

To collect the relevant study characteristics from each publication, a standardized form was used. Using this form, the following data were collected: (a) first author and publication year, (b) design, (c) sample characteristics (clinical characteristics, age, gender, and sample size), (d) outcome type, (e) information on the EMI (training type, training trigger, number of training sessions, and whether training was supported by an MHP), and (f) type of control condition and sample size. When a publication reported on more than one EMI, information was extracted separately for each described EMI, and all EMIs were included separately in the within-subject analyses. For the between-subject analyses, however, only one EMI was included thereby ensuring that each participant is represented only once in the analyses [139]. The EMI that was included in the between-subject analyses was the most 'complete' intervention. In the case of Grassi et al. [134], the Vnar intervention was chosen because it included both video

and audio components compared with a video- or audio-only intervention. For both the studies by Repetto et al. [140] and Pallavicini, Algeri, Repetto, Gorini, and Riva [141], the virtual reality intervention with biofeedback was chosen above the intervention using only virtual reality.

In the meta-analysis, the primary outcome of interest was 'mental health.' Mental health encompasses an anxiety, depression, or stress outcome. Per publication, a set of guidelines was used to determine which specific questionnaire was used to represent this primary outcome. If a study reported one primary outcome, this measure was chosen as an indicator of mental health. When no or multiple primary outcomes were defined, a measure was chosen that was most likely to be affected given the aim of the training. For example, if the training focused on reducing anxiety, then, an anxiety questionnaire was preferred over a questionnaire measuring depression. In this process of selecting questionnaires, comprehensive questionnaires were chosen over restricted questionnaires (if there was such a choice), and the most valid questionnaire was chosen (idem). In addition to the coding of the primary outcome for each publication, the different outcome types per study were also coded. Thus, all questionnaires measuring anxiety, depression, perceived stress, and positive psychological well-being outcomes were listed per publication. A questionnaire was considered to represent positive psychological well-being, when it specifically identified positive emotions or processes that were targeted with the intervention. The only positive psychological well-being outcomes that were identified in the publications were acceptance, feelings of relaxation, and quality of life; positive affect, for instance, was not studied in the included publications. By listing all the questionnaires that measured mental health and positive psychological well-being, it was possible to examine whether the effectiveness of EMI differed per outcome type (e.g., anxiety or depression).

With regard to the information on the EMI, it was reported whether the training was active or passive. A training was labeled as active when participants had to carry out an exercise, for instance, a relaxation exercise [142]. In contrast, a passive training supplied information to the participants (e.g., suggestions or tips) but did not require an immediate action from the participant. For example, participants are given messages that would support self-management [143]. Furthermore, when a trigger (using the EMI device) reminds participants to do the training at a specific moment, the training was coded as 'triggered.' If participants could do the training whenever they preferred, the triggering of the training was said to be 'on-demand.' Moreover, it was reported whether the EMI was used as a stand-alone intervention (coded as stand-alone EMI) or was part of a treatment package and was thus supported by an MHP (coded as MHP-supported EMI). This treatment package could consist of either

an EMI in combination with therapy (e.g., group therapy or exposure therapy) or an EMI with continued feedback (e.g., feedback on homework exercises or messages to improve adherence). An introductory or kickoff session at the start of the intervention was not coded as support. When the effect of an EMI was studied in a population that had access to care as usual (e.g., inpatient or outpatient setting), but this (additional) care was not the focus of the study or was not specifically related to the EMI, the EMI was coded as a stand-alone intervention in combination with care as usual. However, these studies often did not specify whether this available care was used by individuals or what this care specifically entailed. Finally, if a study included a control condition and was therefore eligible for the between-subject analyses, the type of control condition was reported (waitlist, placebo, or active treatment). Specifically, if more than one control condition was used, a placebo condition was chosen over a waitlist condition, and an active treatment control condition was chosen over both the placebo and waitlist condition. When multiple active treatment control conditions were included in the study, the condition was chosen that had the closest resemblance with the EMI condition, but without its 'target ingredient.' This way it was possible to more precisely determine the added value of mobile technology when delivering interventions. Although it is possible to include all reported control conditions using multiple pairwise comparisons (e.g., intervention group vs placebo and intervention group vs waitlist), this yields problems in the analyses as the same group is overrepresented (e.g., twice). Therefore, in the case of the studies of Kenardy et al. [144] and Newman, Przeworski, Consoli, and Taylor [145], the six-session cognitive behavioral therapy (CBT) was chosen to represent the control condition because it better resembled the EMI condition (six sessions of computer-assisted CBT) compared with the 12-session CBT condition. Review author (AV) extracted all the relevant study characteristics from the included publications. To check the inter-rater reliability, a second reviewer (MvdP) assessed data from a subset of the selected papers (i.e., 20%) [146]. For the nominal variables, the average Cohen's kappa was .86 indicating strong agreement between the two raters. The other variables had an 88% (37/42) agreement, which demonstrates a high consistency among raters.

Quality Assessment

The risk of bias in individual studies was assessed using the Cochrane Collaboration tool [147]. This assessment tool uses six different domains for determining the quality of randomized trials: (a) selection bias concerns the method used to generate and conceal the allocation sequence (random sequence generation and allocation concealment, respectively); (b) performance bias deals with ways in which participants and personnel are blinded from knowing condition allocation; (c) detection bias relates to measures

that are taken to blind the outcome assessment from knowledge of which intervention participants received; (d) attrition bias refers to whether the study attrition and exclusions from analysis are reported; (e) reporting bias is whether selective outcome reporting is examined and discussed; (f) other bias refers to any other problems or concerns that are not addressed by previous points. For each publication, the domains are rated with either a 'high' or 'low' risk. If insufficient information is provided in the paper, then, the level of risk is labeled 'unclear.' Higgins et al. [147] argues that within the domain 'other bias,' the sources of bias should be prespecified. In this case, no other biases were specified in advance; therefore, this domain was omitted from the current quality assessment.

The quality assessment was done by the first author (AV), and a 20% sample was assessed by a second reviewer (MvdP). Inter-rater reliability, as assessed with Cohen's kappa, indicated that there was moderate agreement between raters (i.e., average kappa of .69).

Data Analysis

Hedges' *g* was used as an estimate of the effect size. This estimate was calculated using the mean, SD, and sample size at post-intervention as reported in the paper or as based on contact with the authors. Moreover, to compute an effect, a correlation coefficient is needed that represents the correlation between the repeated measures of the outcome parameter. As this within-subject correlation was rarely reported, the correlation was set at .50 for all studies [148]. For interpreting the effect size, the guidelines for Cohen's *d* were used because they are approximately compatible [149]. According to these guidelines, a value of 0.20 is small, 0.50 is medium, and 0.80 is large. Effect sizes are based on a random effect model because we expect the real effect to differ between studies.

To estimate the effect of EMI from pre-intervention to post-intervention, analyses were first run with all within-subject data. Furthermore, to determine whether this effect differed from a control condition, between-subject analyses were run. In both the within- and between-subject analyses, it was determined whether there was an effect on the primary outcome 'mental health' (as measured with a single questionnaire). Second, it was investigated whether the effect differed per outcome type. That is, was the effect of EMI different for anxiety, depression, perceived stress, or positive psychological outcomes (acceptance, relaxation, and quality of life). To determine the effectiveness per outcome type, all relevant outcome types per publication were included in the analysis. When a study used multiple questionnaires to assess an outcome type (e.g., anxiety), an overall mean was created by combining these different

questionnaires. By combining multiple questionnaires per study, the data are unlikely to be independent, and this increases the type II error. Therefore, these analyses are only used to explore whether there are potential differences in effects between the outcome types. In addition, for the primary outcome 'mental health,' subgroup analyses are done to determine whether the effect differed as a function of design (randomized controlled trial [RCT] or pre-post), sample (healthy or clinical), age, gender, sample size, training type (active or passive), training trigger (triggered, on-demand, or unspecified), daily training sessions (number), total training sessions (number), support by MHP (stand-alone EMI, MHP-supported EMI, or stand-alone EMI with access to care as usual), and quality assessment (0-6). Year of publication was not included as a moderator because there was little variation in this variable (i.e., 25 of the 32 publications were published in 2010 or later). Moreover, type of control condition was not included as a moderator because only 13 studies had a between-subject design.

As a measure of heterogeneity, the *Q* and I^2 statistics were used. A significant *Q*-statistic indicates that there is variation in the true effect size, and I^2 reflects the amount of real variance—specifically, values of 25%, 50%, and 75% can be considered small, medium, and large values, respectively [150]. Moreover, the risk for publication bias was examined using different techniques [139]. First, the distribution in the funnel plot was visually inspected as a preliminary indication for publication bias. This plot represents the effect size against the standard error of the study. Generally, studies with a large sample size are represented at the top of the plot around the mean, and studies with a smaller sample size are located at the bottom of the plot with a wider distribution around the mean. In the case of publication bias, studies with a small sample size are more likely to fall to the right of the mean (indicating a positive effect size). In other words, when the distribution of studies becomes asymmetrical, there is indication for publication bias. To quantify the amount of bias, the Egger's test of intercept was used. In this approach, the amount of bias is captured in the intercept value, and a significant intercept indicates that there is significant publication bias. Furthermore, to correct for the missing studies (to the left of the mean), a Duval and Tweedie's trim and fill method was used. This method calculates where missing studies were most likely to fall and adds these studies to the analysis. The recomputed effect size and CI are thereby corrected for the missing studies and is assumed to be unbiased [139].

Outliers were identified using the value of the standardized residual in both the within- and between-subject analyses. Studies whose standardized residual was significant (values ± 1.96) were excluded from the analyses.

The software Comprehensive Meta-Analysis version 3.3.070 (Biostat) was used for all the described analyses including the calculation of effect sizes with 95%

CIs. The forest plots were made using the metaphor package in R (version 3.0.3) [151].

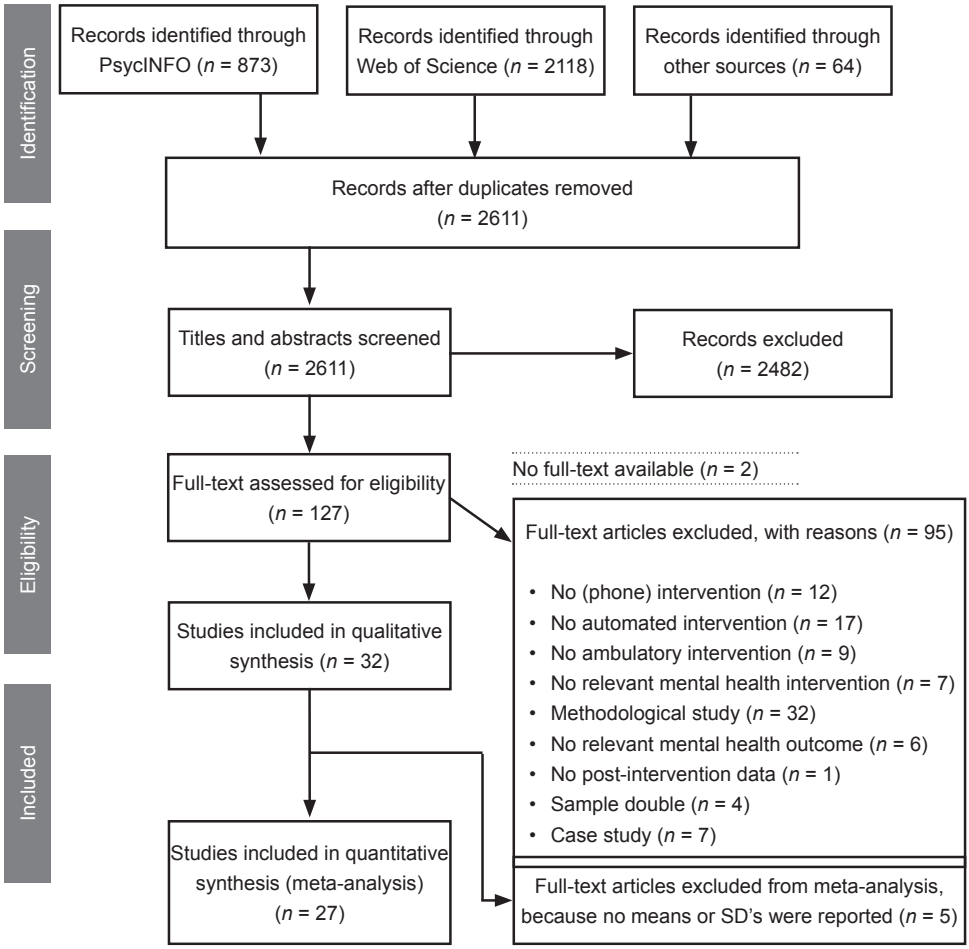

FIGURE 1 Flow diagram for study inclusion

RESULTS

A total of 2611 publications were identified with the search strategies after removing duplicates (see Figure 1) [138]. After screening the titles and abstracts, 127 full-text publications were screened for eligibility. Most of these publications were excluded because no (mobile phone) intervention was studied, the intervention was not automated (i.e., not independent from therapist), or no outcome data were discussed

(methodological paper). A total of 32 publications were considered relevant and were included in the analysis (see Tables 1 and 2). In these 32 publications, 33 different studies were reported using 43 samples that received an EMI (n = 1301). The included study by Huffziger et al. [135] was technically an ecological momentary assessment study (with an experimental manipulation) and not an EMI. However, considering that the manipulation that was used (mindfulness attention induction) can be seen as an intervention, the study was included.

For the meta-analysis, five publications were excluded because no means and SDs to calculate the effect size were reported or obtained after contacting the authors [152-156]. Therefore, 27 publications (27 studies) with 33 samples that received an EMI were included in the meta-analysis (n = 1156).

TABLE 1 Characteristics of the ecological momentary intervention studies (part 1)

Study[a]	Design[b]	Sample	Age (years)	Gender (% female)	*n*[c]	Mental Health Measure[d]	Outcome type(s)
Included in meta-analysis							
Agyapong et al, 2012[e]	RCT	Clinical	48.00	54	24	BDI	Depression
Ahtinen et al, 2013	Pre-post	Healthy	—	60	14	Stress single-item	Stress Acceptance Quality of life
Aikens et al. 2015[f] (all pooled subjects)	Pre-post	Clinical	51.40	79	221	PHQ-8	Depression
Askins et al, 2009	RCT	Healthy	36.30	100	64	POMS	Depression
Ben-Zeev et al, 2014	Pre-post	Clinical	45.90	39w	32	BDI	Depression
Burns et al, 2011[e]	Pre-post	Clinical	37.40	88	7	GIDS-c	Depression Anxiety
Carissoli et al, 2015	RCT	Healthy	38.11	57	20	MSP	Stress
Dagöö et al. 2014[g] (mCBT)	RCT	Clinical	34.70	48	24	LSAS-SR	Depression Anxiety Quality of life
Dagöö et al, 2014[g] (mIPT)	RCT	Clinical	39.08	56	19	LSAS-SR	Depression Anxiety Quality of life
Depp et al, 2015	RCT	Clinical	46.90	54	41	MADRS	Depression

Study[a]	Design[b]	Sample	Age (years)	Gender (% female)	*n*[c]	Mental Health Measure[d]	Outcome type(s)
Enock et al. 2014	RCT	Clinical	34.80	48	120	SIAS	Depression Anxiety
Granholm et al, 2012	Pre-post	Clinical	48.70	31	41	BDI	Depression
Grassi et al, 2007 (Vnar)	Pre-post[h]	Healthy	23.27	50	30	STAI-state	Anxiety Relaxation
Grassi et al, 2007 (Nnar)	Pre-post[h]	Healthy	23.27	50	30	STAI-state	Anxiety Relaxation
Grassi et al, 2007[e] (MP3)	Pre-post[h]	Healthy	23.27	50	30	STAI-state	Anxiety Relaxation
Harrison et al, 2011	Pre-post	Clinical	38.20	71	28	DASS total score	Depression Anxiety
Huffziger et al, 2013[i]	Pre-post	Healthy	22.90	60	46	Valence 2-items	Depression Relaxation
Kenardy et al, 2003[e]	RCT	Clinical	36.80	76	41	Anxiety composite score	Anxiety
Lappalainen et al, 2013	RCT	Clinical	47.10	0	11	GSI	Depression Acceptance Quality of life
Ly et al, 2014[e] (behavioral activation)	RCT	Clinical	36.60	70	36	BDI	Depression Anxiety Acceptance Quality of life
Ly et al, 2014 (mindfulness)	RCT	Clinical	35.60	71	36	BDI	Depression Anxiety Acceptance Quality of life
Ly et al, 2012	Pre-post	Healthy	29.50	36	11	DASS stress	Depression Anxiety Stress Quality of life
Newman et al, 2014	RCT	Clinical	42.45	55	11	STAI—trait	Anxiety
Newman et al, 1997	RCT	Clinical	38.00	83	9	FQ—total score	Anxiety
Pallavicini et al, 2009 (VRMB)	Pre-post[h]	Clinical	41.25	—	4	GAD7	Anxiety
Pallavicini et al, 2009 (VRM)	Pre-post[h]	Clinical	48.50	—	4	GAD7	Anxiety

Study[a]	Design[b]	Sample	Age (years)	Gender (% female)	*n*[c]	Mental Health Measure[d]	Outcome type(s)
Proudfoot et al, 2013	RCT	Clinical	39.00	70	126	DASS total score	Depression Anxiety Stress
Repetto et al, 2013 (VRMB)	Pre-post[h]	Clinical	—	64	7	BAI	Anxiety
Repetto et al, 2013 (VRM)	Pre-post[h]	Clinical	—	64	9	BAI	Anxiety
Rizvi et al, 2011	Pre-post	Clinical	33.86	82	22	BSI	Depression
Shapiro et al, 2010	Pre-post	Clinical	26.30	100	14	BDI	Depression
Watts et al, 2013[e]	RCT	Clinical	41.00	80	10	BDI	Depression Stress
Wenze et al, 2014	Pre-post	Clinical	40.86	71	14	QIDS-c	Depression
Not included in meta-analysis							
Gorini et al, 2010 (VRMB)	Pre-post[h]	Clinical	—	—	8	BAI	Anxiety
Gorini et al, 2010 (VRM)	Pre-post[h]	Clinical	—	—	4	BAI	Anxiety
Grassi et al, 2011 (Vnar)	Pre-post[h]	Healthy	20.86	100	15	STAI-state	Anxiety Relaxation
Grassi et al, 2011 (MP3)	Pre-post[h]	Healthy	20.86	100	15	STAI-state	Anxiety Relaxation
Preziosa et al, 2009 (Vnar; study 1)	Pre-post	Healthy	23.48	100	6	STAI-state	Anxiety Depression
Preziosa et al, 2009 (MP3; study 1)	Pre-post	Healthy	23.48	100	6	STAI-state	Anxiety Depression
Preziosa et al, 2009 (study 2)	RCT	Healthy	23.48	50	30	STAI-state	Anxiety Depression Relaxation
Riva et al, 2006	RCT	Healthy	23.82	48	11	STAI-state	Anxiety Depression Relaxation
Zautra et al, 2012 (mindfulness)	RCT	Clinical	54.05	82	25	Depression 3-items	Depression Stress
Zautra et al, 2012 (mastery-control)	RCT	Clinical	54.05	82	25	Depression 3-items	Depression stress

[a]Studies are ordered by inclusion in the meta-analysis. Behind the study's year of publication, between brackets, the sample (or condition) that received the ecological momentary intervention was specified; With mCBT: mobile cognitive behavioral therapy; mIPT: mobile interpersonal psychotherapy; MP3: audio only condition; Nnar: video only condition VRMB: virtual reality and mobile condition with biofeedback; VRM: virtual reality with mobile condition; Vnar: video narrative condition.

[b]Design of study is labeled either randomized controlled trial (RCT) or pre-post design.
[c]Sample size at post-intervention in the condition receiving the ecological momentary intervention.
[d]The specific questionnaire that was used to represent the primary outcome 'mental health' is listed. With BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; BSI: Brief Symptom Inventory; DASS: Depression Anxiety Stress Scales; FQ: Fear Questionnaire; GAD7: Generalized Anxiety Disorder 7-item; GIDS-c: Quick Inventory of Depressive Symptoms-Clinician rated; GSI: General Symptom Index; LSAS-SR: Liebowitz Social Anxiety Scale Self-Report; MADRS: Montgomery–Åsberg Depression Rating Scale; MSP: Mesure du Stress Psychologique; PHQ-8: Patient Health Questionnaire Depression scale; POMS: Profile of Mood States; SIAS: Social Interaction Anxiety Scale; STAI: State-Trait Anxiety Inventory.
[e]Study is considered an outlier in within-subject analyses.
[f]The data used for the analyses consists of all pooled participants, the outcome questionnaire at pre-intervention is compared with last outcome questionnaire that the participant completed.
[g]The intervention could be accessed using the mobile phone, tablet, and computer.
[h]Study is labeled as a pre-post design, because it is unclear whether participants were randomized across conditions.
[i]The study is technically an ecological momentary assessment study with an experimental manipulation.

TABLE 2 Characteristics of the ecological momentary intervention studies (part 2)

Study[a]	Intervention technique	Training type (+ type of MHP[b] support[c])	Training trigger	No. of training sessions[d]	Control (*n*)[e]
Included in meta-analysis					
Agyapong et al, 2012[f]	Self-management and monitoring	Passive (stand-alone + CAU)	Triggered	168 (2)	Waitlist (*n*=28)
Ahtinen et al, 2013	Acceptance and commitment therapy	Active	On-demand		
Aikens et al, 2015[g] (all pooled subjects)	Self-management and monitoring	Passive (+MHP)	Triggered	26 (1)	
Askins et al, 2009	Self-management and monitoring	Active (+MHP)	—	—	
Ben-Zeev et al, 2014	Self-management and monitoring	Active (+stand-alone + CAU)	Triggered	90 (3)	
Burns et al, 2011[f]	Behavioral activation	Active (+MHP)	Triggered	280 (5)	
Carissoli et al, 2015	Mindfulness	Active	On-demand	36 (2)	Placebo (*n*=18)
Dagöö et al, 2014[h] (mCBT[b])	Cognitive behavioral therapy	Active (+MHP)	—	—	
Dagöö et al 2014[h] (mIPT[b])	Interpersonal therapy	Active (+MHP)	—	—	

Study[a]	Intervention technique	Training type (+ type of MHP[b] support[c])	Training trigger	No. of training sessions[d]	Control (*n*)[e]
Depp et al, 2015	Self-management and monitoring	Passive (+MHP)	Triggered	140 (2)	Paper and pencil version (*n*=41)
Enock et al, 2014	Cognitive bias modification	Active	Triggered	84 (3)	Placebo (*n*=104)
Granholm et al, 2012	Cognitive behavioral therapy	Active (stand-alone + CAU)	Triggered	216 (3)	
Grassi et al, 2007 (Vnar[b])	Relaxation	Active	—	4 (2)	Waitlist (*n*=30)
Grassi et al, 2007 (Nnar[b])	Relaxation	Active	—	4 (2)	
Grassi et al, 2007[f] (MP3[b])	Relaxation	Active	—	4 (2)	
Harrison et al, 2011	Self-management and monitoring	Passive	On-demand	—	
Huffziger et al, 2013[i]	Mindfulness	Passive	Triggered	10 (10)	
Kenardy et al, 2003[f]	Cognitive behavioral therapy	Active (+MHP)	Triggered	420 (5)	CBT6 (*n*=44)
Lappalainen et al, 2013	Cognitive behavioral therapy and acceptance and commitment therapy	Active (+MHP)	On-demand	—	Waitlist (*n*=12)
Ly et al, 2014[f] behavioral activation	Behavioral activation	Active (+MHP)	—	—	
Ly et al, 2014 mindfulness	Mindfulness	Active (+MHP)	—	—	
Ly et al, 2012	Acceptance and commitment therapy	Active	On-demand	—	
Newman et al, 2014	Cognitive behavioral therapy	Active (+MHP)	Triggered	112 (4)	CBT6 (*n*=14)
Newman et al, 1997	Cognitive behavioral therapy	Active (+MHP)	Triggered	336 (4)	CBT12 (*n*=9)
Pallavicini et al, 2009 (VRMB[b])	Relaxation	Active (+MHP)	On-demand	—	Waitlist (*n*=4)
Pallavicini et al, 2009 (VRM[b])	Relaxation	Active (+MHP)	On-demand	—	

Study[a]	Intervention technique	Training type (+ type of MHP[b] support[c])	Training trigger	No. of training sessions[d]	Control (*n*)[e]
Proudfoot et al, 2013	Self-management and monitoring	Passive	On-demand	—	Placebo (*n*=195)
Repetto et al, 2013 (VRMB)	Relaxation	Active (+MHP)	On-demand	—	Waitlist (*n*=8)
Repetto et al, 2013 (VRM)	Relaxation	Active (+MHP)	On-demand	—	
Rizvi et al, 2011	Dialectical behavior therapy	Active (+TAU)	On-demand	—	
Shapiro et al, 2010	Self-management and monitoring	Passive (+MHP)	—	168 (1)	
Watts et al, 2013[f]	Cognitive behavioral therapy	Active (+MHP)	On-demand	—	Computer version (*n*=15)
Wenze et al, 2014	Cognitive behavioral therapy	Passive (stand-alone + CAU	Triggered	28 (2)	
Not included in meta-analysis					
Gorini et al, 2010 (VRMB)	Relaxation	Active (+MHP)	On-demand	—	Waitlist (*n*=8)
Gorini et al, 2010 (VRM)	Relaxation	Active (+MHP)	On-demand	—	
Grassi et al, 2011 (Vnar)	Relaxation	Active	—	6 (1)	Waitlist (*n*=15)
Grassi et al, 2011 (MP3[b])	Relaxation	Active	—	6 (1)	
Preziosa et al, 2009 (Vnar; study 1)	Relaxation	Active	—	6 (1)	Waitlist (*n*=6)
Preziosa et al, 2009 (MP3; study 1)	Relaxation	Active	—	6 (1)	
Riva et al, 2006	Relaxation	Active	—	4 (2)	Placebo (*n*=30)
Preziosa et al, 2009 (study 2)	Relaxation	Active	—	4 (2)	Placebo (*n*=11)
Zautra et al, 2012 (mindfulness)	Mindfulness	Active	Triggered	27 (1)	Placebo (*n*=23)
Zautra et al, 2012 (mastery-control)	Behavioral activation	Active	Triggered	27 (1)	

[a]Studies are ordered by inclusion in the meta-analysis. Behind the study's year of publication, between brackets, the sample (or condition) that received the ecological momentary intervention was specified.

[b]mCBT: mobile cognitive behavioral therapy; mIPT: mobile interpersonal psychotherapy; MP3: audio only condition; MHP: mental health professional; Nnar: video only condition; Vnar: video narrative condition;

VRMB: virtual reality and mobile condition with biofeedback; VRM: virtual reality with mobile condition.

[c] Following the type of training, the type of support by the mental health professional is reported between brackets. With +MHP = mental health professional–supported EMI; stand-alone + CAU = stand-alone EMI with access to care as usual. No information was displayed when the EMI was stand-alone.

[d]The maximum number of total training sessions is reported. The maximum number of daily training sessions is reported between brackets.

[e] Control condition (and sample size at post-intervention) is listed if the study was included in the between-subject analyses. If the control condition is an active treatment, it is specified which specific active treatment condition is used to calculate the effect size. With CBT6 = 6-sessions of cognitive behavioral therapy; CBT12 = 12-sessions of cognitive behavioral therapy.

[f] Study is considered an outlier in within-subject analyses.

[g]The data used for the analyses consists of all pooled participants, the outcome questionnaire at pre-intervention is compared with last outcome questionnaire that the participant completed.

[h]The intervention could be accessed using the mobile phone, tablet, and computer.

[i]The study is technically an ecological momentary assessment study with an experimental manipulation.

Study Characteristics

Of the 33 studies that were included, 17 had a pre-post design, and 16 studies were an RCT. Of the total number of studies, 10 included healthy individuals [134, 135, 142, 153, 157-160] (studies 1 and 2 [154]), and the remaining studies focused on a clinical sample. Specifically, the focus of eight studies was on anxiety disorders [140, 141, 144, 145, 152, 161-163], six on depressive symptoms (ranging from mild symptoms to major depressive disorder) [143, 156, 164-167], one on perceived stress [168], two on anxiety, depression, and stress [169, 170], two on bipolar disorder [171, 172], two on schizophrenia [159, 173], one on borderline personality disorder [174], and one on bulimia nervosa [175]. No study had positive psychological well-being as primary outcome. Across the studies, the average age ranged from 20.86 to 54.05 years with a mean of 37.33 (SD = 9.37). Only female participants were included in four studies [153, 157, 175] (study 1 [154]), one study included only males [168], and overall, the percentage of females was 64.79 (SD = 22.72).

Intervention Characteristics

A range of different intervention techniques were studied: CBT [144, 145, 159, 161, 163, 167, 168, 172], acceptance and commitment therapy [142, 160, 168], mindfulness [135, 156, 158, 166], behavioral activation [156, 165, 166], relaxation [134, 140, 141, 152-155], interpersonal therapy [161], dialectical behavior therapy [174], cognitive bias modification [162], and self-management and/or monitoring strategies [143, 157, 164, 169-171, 173, 175]. The EMI was offered in combination with therapy in 10 studies

(30%). Four studies combined the EMI with CBT [144, 145, 163, 175], three with virtual reality including both relaxation and exposure [140, 141, 152], one with a problem-skill training [157], one with psychoeducation [171], and one with meetings including mindfulness and acceptance exercises [168]. In five studies, the EMI was a stand-alone intervention in combination with care as usual. This care focused on bipolar disorder [172], schizophrenia or schizoaffective disorder [159, 173], major depressive disorder, and alcohol dependency [164], or on borderline personality disorder and substance abuse [174]. The other 18 studies investigated whether the use of an individual EMI can be effective without face-to-face therapy confounding the effect. Nevertheless, support by an MHP was included in five of these 18 studies. The MHP was, for instance, used to support the participant in the first phase of the intervention [167], to give feedback on the homework using Internet or email [161, 166], or to increase adherence by telephone [143, 165]. As can be seen in Table 2, 13 studies (39%) did not include support by an MHP after starting the EMI. In addition to the EMI and the potential support offered by the MHP, six of the 33 studies used a website for psychoeducation [160, 166] or for providing therapy modules [165, 168-170]. Most of the EMIs under investigation were 'active' (25/33, 76%), meaning that participants had to carry out an exercise as part of the intervention. The EMIs in the remaining studies were classified as passive and only provided the participant with information.

On average, the EMI lasted for 7.47 weeks (SD = 6.46), but this varied considerably. For example, the studies with the shortest EMI lasted only one or two days [134, 135, 155] (study 2 [154]), whereas the study with the longest EMI lasted for 26 weeks [143]. However, these numbers may be only modestly informative considering that the number of training sessions that people received (per day) varied highly across the studies. To explain, the study with the shortest length of training actually had the highest number of training sessions per day [135], whereas the study with the longest training length only trained people once a week [143]. Therefore, it may be more valuable to examine how many training sessions participants received per day and in total. Unfortunately, 13 studies did not specify the number of training sessions (per day or in total). Across the 20 other studies, the average number of training sessions was 2.80 per day (SD = 2.12) ranging from 1 to 10, and on average 108.25 in total (SD = 123.00) ranging from 4 to 420. The number of training sessions not only varied across studies but likely also varied across individuals within a given study. Fifteen of the 33 studies (i.e., 45%) reported (some) information about compliance with the training, but the information used to represent compliance differed across studies. The average compliance with the sessions or treatment modules was 73.88% (SD = 16.73) [135, 156, 159, 161, 162, 166, 167, 169, 171, 172, 175]. Burns et al. [165] reported that the

number of training sessions was on average 15.30 (SD = 8.30) in the first week and that this decreased to 9.00 (SD = 6.50) in the final week. In study of Ben-Zeev et al. [173], participants used the training on 86.50% of the days and on these days used on average 5.19 sessions. Participants in the study by Aikens et al. [143] participated in a median of 25 weeks (of the 26 weeks). Finally, Lappalainen et al. [168] disclosed that all participants tried at least three out of the six available tools; however, no data are reported on the frequency of use.

The training sessions were automatically triggered by the device in 13 studies, and in 11 studies, the training sessions were not specifically triggered, and participants could complete the training whenever they wanted. Nine studies did not report whether the training was triggered or whether it was accessed on-demand.

Quality Assessment

The quality assessment of the studies is summarized in Table 3 and is on average 2.29 (SD = 1.42, NB on a scale from 0 to 6), which can be considered low. Nine studies had a pre-intervention to post-intervention design, so the quality domain 'selection bias'—as indexed by 'random sequence generation' and 'allocation concealment'—was not applicable (quality domain 1, see the previous section) [142, 159, 160, 165, 169, 172-175]. Only four studies had a low risk of bias on this domain [161, 166, 167, 171], with five other studies having a low risk of bias on 'random sequence generation' and an unclear or high risk on 'allocation concealment' [135, 140, 141, 157, 164]. In the remaining 14 studies, the risk was either unclear or high. The blinding of personnel (domain 2) was achieved in only two studies [170, 171]. Moreover, most studies used self-report questionnaires, with only two studies using clinician-rated interviews (domain 3)—however, clinicians were not blinded for the condition of the participants [165, 172]. There was a high risk for attrition (domain 4; i.e., ≥ 20%) in eight studies [157, 159, 162, 167, 169-171, 175], and attrition (in the EMI group) was not disclosed in seven studies [134, 144, 152, 153, 155] (studies 1 and 2 [154]). Finally, seven studies failed to report the results for all prespecified outcome types (domain 5) [134, 141, 152, 153, 155] (studies 1 and 2 [154]).

TABLE 3 Quality assessment of the individual studies using the Cochrane Collaboration's tool

Study	Random sequence generation[a]	Allocation concealment[a]	Performance bias[b]	Detection bias	Attrition bias[c]	Reporting bias[d]	Overall grade[e]
Agyapong et al, 2012	+	−	−	−	+	+	3
Ahtinen et al, 2013	N/A	N/A	−	−	+	+	4
Aikens et al, 2015	−	−	−	−	+	+	2
Askins et al, 2009	+	?	−	−	−	+	2
Ben-Zeev et al, 2014	N/A	N/A	−	−	+	+	4
Burns et al, 2011	N/A	N/A	−	?	+	+	4
Carissoli et al, 2015	?	?	−	−	+	+	2
Dagöö et al, 2014	+	+	−	−	+	+	4
Depp et al, 2015	+	+	+	−	−	+	4
Enock et al, 2014	?	?	?	−	−	+	1
Gorini et al, 2010[f]	?	?	−	−	?	−	0
Granholm et al, 2012	N/A	N/A	−	−	−	+	3
Grassi et al, 2011[f]	?	?	−	−	?	−	0
Grassi et al, 2007	?	?	−	−	?	−	0
Harrison et al, 2011	N/A	N/A	−	−	−	+	3
Huffziger et al, 2013	+	?	−	−	+	+	3
Kenardy et al, 2003	?	?	−	−	?	+	1
Lappalainen et al, 2013	?	?	−	−	+	+	2
Ly et al, 2014	+	+	−	−	+	+	4
Ly et al, 2012	N/A	N/A	−	−	+	+	4
Newman et al, 2014	?	?	−	−	+	+	2
Newman et al, 1997	?	?	−	−	+	+	2
Pallavicini et al, 2009	+	?	−	−	+	−	2
Preziosa et al, 2009[f] (studies 1 and 2)	?	?	−	−	?	−	0
Proudfoot et al, 2013	+	+	+	−	−	+	4
Repetto et al, 2013	+	?	−	−	+	−	2
Riva et al, 2006[f]	?	?	−	−	?	−	0
Rizvi et al, 2011	N/A	N/A	−	−	+	+	4
Shapiro et al, 2010	N/A	N/A	−	−	−	+	3
Watts et al. 2013	+	+	−	−	−	+	3
Wenze et al, 2014	N/A	N/A	−	?	+	+	4
Zautra et al, 2012[f]	?	?	−	−	+	+	2

[a]The label “not applicable” (N/A) is used in one-armed studies.
[b]The risk for performance bias is rated low if personnel are blinded irrespective of whether participants were blinded.
[c]The bias for attrition is considered high when the attrition from pre-intervention to post-intervention is 20% or more.
[d]The bias for selective reporting is labeled low if all prespecified outcomes are reported, it is not necessary that all statistical information is reported per outcome (e.g., means, standard deviation, CI, *p* values).
[e]The overall grade is determined by summing the number of low-risk categories and the number of N/A categories; + = low risk of bias; − = high risk of bias; ? = unclear risk of bias.
[f]Study is not included in the meta-analysis.

Within-Subject Analyses

A total of 27 publications including 33 EMI groups (n = 1156), were included in the within-subject analyses, and these studies had significant heterogeneity, $Q(32)$ = 188.80 with $p < .001$. The I^2 statistic showed that the observed variance was high (I^2 = 83.05). This further supports the use of a random effect model in the analyses.

The average effect on mental health from pre-intervention to post-intervention was g = 0.73, 95% CI (0.56, 0.90), $p < .001$ (see Figure 2 and Table 4), indicating a medium to large effect. To determine whether there was a risk for publication bias, the distribution in the funnel plot was examined. As can be seen in Figure 3, most of the studies (white circles) are centered at the top of the plot and are distributed to the right side of the mean as the sample size decreases. This reflects the presence of a publication bias, and an Egger’s test of intercept was used as a method to quantify the amount of bias. In this case, the intercept was 1.89, 95% CI (0.28, 3.51), with $t(31)$ = 2.39 and one-sided p = .010. In other words, there was a significant risk for bias. To correct for the missing studies to the left of the mean, the trim and fill method was used. Figure 3 shows that 2 studies (black circles) were added and the corrected effect size was g = 0.70, 95% CI (0.52, 0.87). The corrected effect is virtually identical to the unadjusted effect, which suggests that the reported findings are quite robust and are not simply due to publication bias.

The standardized residual identified six studies as outliers, and these were removed from the analyses [144, 164, 165, 167] (MP3 condition [134]) (BA condition [166]). Removal of these studies resulted in a decrease in effect and heterogeneity (g = 0.57, 95% CI [0.45, 0.70], $p < .001$; $Q(26)$ = 74.46, I^2 = 65.08). Nevertheless, the effect was still medium for the 27 included EMI groups (n = 1008), and the studies were significantly heterogeneous.

It was explored whether the effect was different per outcome type. Depressive symptoms were assessed in 17 studies; anxiety in 15 studies; quality of life in 6 studies; stress in 5 studies; acceptance in 4 studies, and relaxation in 3 studies. As can be seen

in Table 5, there was evidence for an effect on anxiety (g = 0.47, 95% CI [0.32, 0.63], p < .001), depression (g = 0.48, 95% CI [0.34, 0.61, p < .001), perceived stress (g = 0.40, 95% CI [0.23, 0.57], p < .001), acceptance (g = 0.36, 95% CI [0.13, 0.59], p = .002), and quality of life (g = 0.38, 95% CI [0.19, 0.56], p < .001). No effect was found on relaxation with g = 0.28, 95% CI (−0.46, 1.01), p = .461. However, there was no evidence that the effect differed significantly per outcome type with $Q(5) = 1.74$, p = .880.

Furthermore, subgroup analyses were done to see whether the effect varied by moderator. Table 4 shows that 'support by an MHP' was the only moderator for which the effect varied significantly, $Q(2) = 6.77$, p =.030. Specifically, the effect was medium to large when the EMI included support by an MHP (g = 0.73, 95% CI [0.57, 0.88]), small to medium for the stand-alone EMI (g = 0.45, 95% CI [0.22, 0.69]), and small for those individuals who received a stand-alone EMI in combination with care as usual (g = 0.38, 95% CI [0.11, 0.64]).

TABLE 4 Effect sizes (Hedges' g) of ecological momentary intervention on mental health by study and intervention characteristics (within-subject analyses)[a]

	Random effect model			Heterogeneity		Test of difference
Outcome	k[b]	n[c]	g (95% CI)[d]	Q[e]	I^2[e]	Q[f]
Mental health	27	1008	0.57 (0.45, 0.70)[g]	74.46[g]	65.08	
Design						1.03
RCT[h]	11	481	0.65 (0.48, 0.82)[g]	24.10[i]	58.50	
Pre-post	16	527	0.52 (0.33, 0.71)[g]	47.34[g]	68.32	
Sample						1.79
Clinical	20	793	0.63 (0.50, 0.76)[g]	39.32[i]	51.68	
Healthy	7	215	0.40 (0.10, 0.71)[j]	26.76[g]	77.58	
Age[k], years						2.19
≤ 38.15	12	426	0.61 (0.36, 0.86)[g]	54.38[g]	79.77	
> 38.15	12	552	0.51 (0.37, 0.64)[g]	17.64[l]	37.65	
Unspecified	3	30	0.80 (0.41, 1.18)[g]	0.40	0.00	
Gender[k]						1.96
≤ 60% female	14	450	0.49 (0.28, 0.70)[g]	51.25[g]	74.63	
> 60% female	11	550	0.67 (0.53, 0.81)[g]	15.94	37.26	
Unspecified	2	8	0.55 (−0.08, 1.17)[j]	1.12	10.43	
Sample size[k]						1.18
≤ 22 participants	13	158	0.67 (0.46, 0.87)[g]	17.24	30.39	
> 22 participants	14	850	0.52 (0.36, 0.69)[g]	56.36[g]	76.93	
Training type						0.32
Active	20	518	0.60 (0.42, 0.78)[g]	57.51[g]	66.96	
Passive	7	490	0.53 (0.34, 0.71)[g]	16.65[j]	63.97	

Outcome	Random effect model			Heterogeneity		Test of difference
	k[b]	*n*[c]	*g* (95% CI)[d]	*Q*[e]	*I*[e]	*Q*[f]
Training trigger						1.65
Triggered	9	535	0.52 (0.33, 0.71)[g]	26.96[i]	70.45	
On-demand	11	256	0.49 (0.37, 0.62)[g]	9.41	0.00	
Unspecified	7	217	0.76 (0.38, 1.14)[g]	35.69[g]	83.19	
No. of daily training sessions[k]						0.53
≤ 2	7	370	0.55 (0.24, 0.87)[i]	32.65[g]	81.62	
> 2	6	259	0.51 (0.20, 0.82)[i]	22.81[g]	78.08	
Unspecified	14	379	0.63 (0.49, 0.77)[g]	17.48	25.62	
No. of total training sessions[k]						0.92
≤ 84	7	481	0.48 (0.21, 0.75)[i]	36.62[g]	83.62	
> 84	6	148	0.62 (0.27, 0.97)[i]	17.77[i]	71.86	
Unspecified	14	379	0.63 (0.49, 0.77)[g]	17.48	25.62	
Support MHP[m]						6.77[j]
MHP-supported EMI	14	474	0.73 (0.57, 0.88)[g]	20.67[l]	37.10	
Stand-alone EMI	9	425	0.45 (0.22, 0.69)[g]	35.81[j]	77.66	
Stand-alone EMI with access to care as usual	4	109	0.38 (0.11, 0.64)[i]	5.37	43.97	
Quality assessment[k]						0.01
≤ 3	17	781	0.57 (0.39, 0.76)[g]	57.68[j]	72.26	
> 3	10	227	0.59 (0.42, 0.76)[g]	16.78[l]	46.38	

[a]Outliers were excluded from the presented moderation analyses (i.e., 6 studies).
[b]*k* = number of studies.
[c]*n* = number of participants.
[d]*g* = effect size Hedges' *g* with 95% CI.
[e]*Q* and I^2 = heterogeneity statistics.
[f]*Q* = contrast between subgroups.
[g]$p < .001$.
[h]RCT = randomized controlled trial.
[i]$p < .01$.
[j]$p < .05$.
[k]Data were categorized based on the median.
[l]$p < .10$.
[m]MHP = mental health professional.

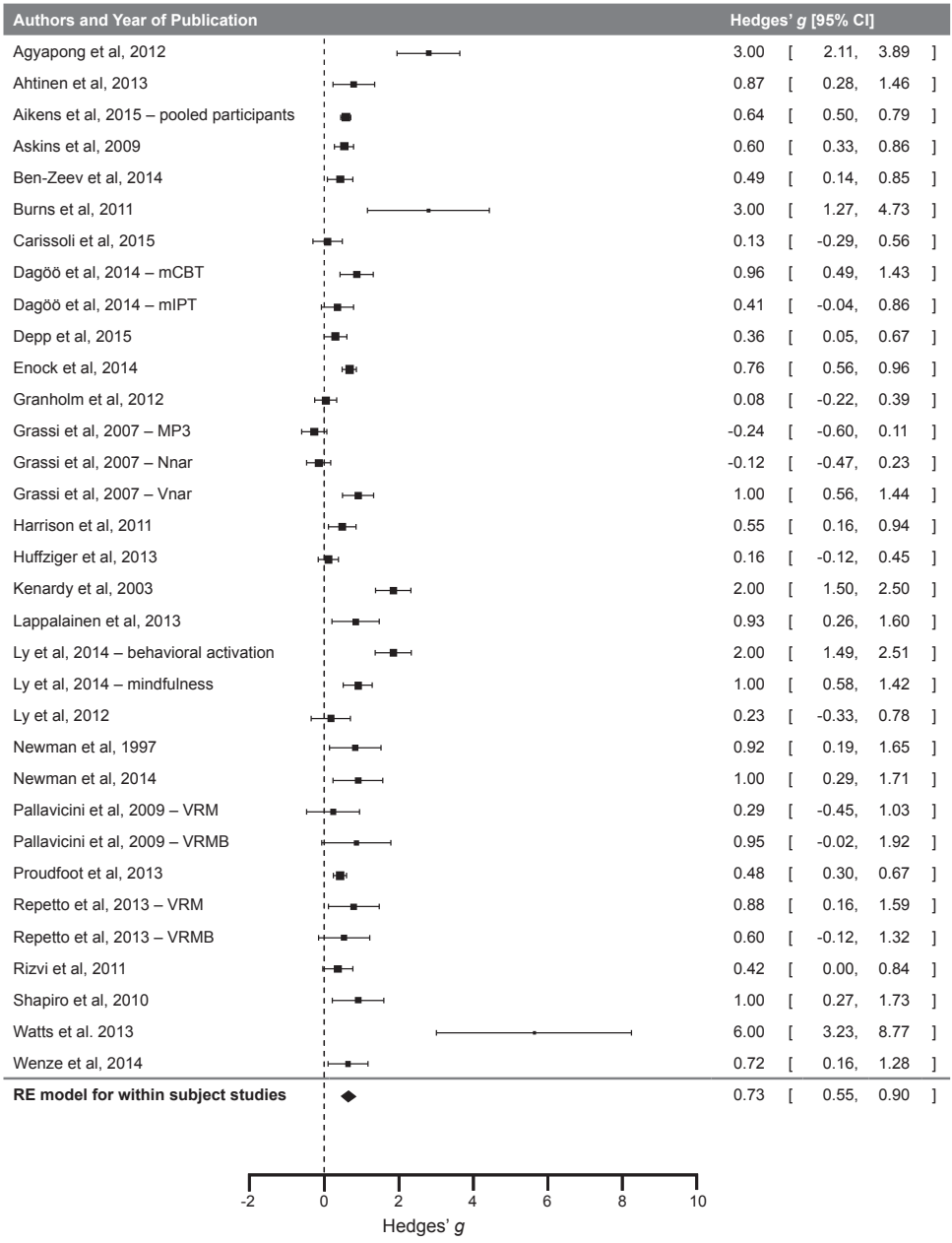

Figure 2 Forest plot showing the effect of ecological momentary interventions (EMIs) on mental health complaints for all within-subject studies. The EMI sample (or condition) is reported after the year of publication when multiple EMI samples were included in a publication

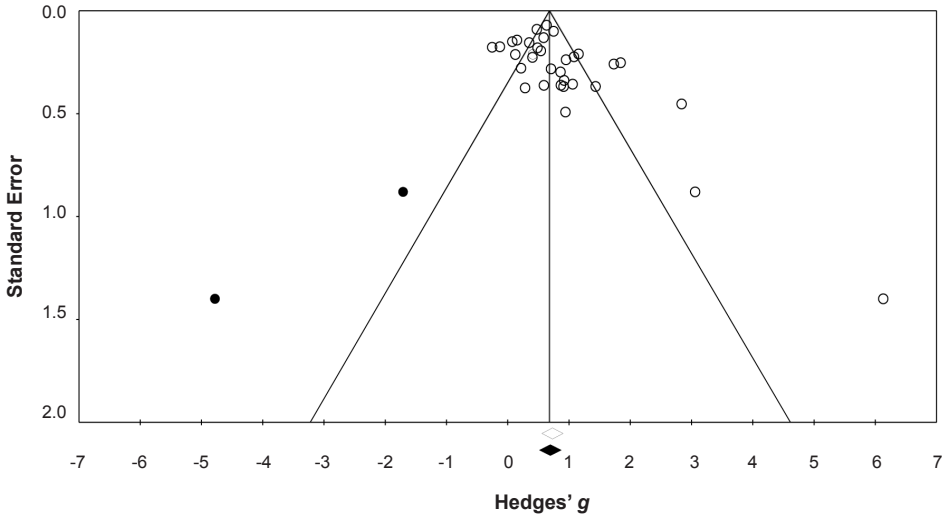

FIGURE 3 Funnel plot of standard error by Hedges' *g* with imputed values based on Duval and Tweedie's trim and fill method (within-subject studies)

TABLE 5 Effect sizes (Hedges' *g*) of ecological momentary intervention by outcome type (within-subject analyses)[a]

	Random effect model			Heterogeneity		Test of difference
Outcome	*k*[b]	*n*[c]	*g* (95% CI)[d]	*Q*[e]	I^2[e]	*Q*[f]
Overall	50	1830				1.74
Anxiety	15	468	0.47 (0.32, 0.63)[g]	28.28[h]	50.49	
Depression	17	870	0.48 (0.34, 0.61)[g]	46.48[g]	65.58	
Perceived stress	5	199	0.40 (0.23, 0.57)[g]	4.59	12.79	
Relaxation	3	106	0.28 (−0.46, 1.01)	25.28[g]	92.09	
Acceptance	4	72	0.36 (0.13, 0.59)[i]	2.79	0.00	
Quality of life	6	115	0.38 (0.19, 0.56)[g]	4.25	0.00	

[a]Outliers were excluded from the presented moderation analyses (i.e., 6 studies).

[b]*k* = number of studies.

[c]*n* = number of participants.

[d]*g* = effect size Hedges' *g* with 95% confidence interval.

[e]*Q* and I^2 = heterogeneity statistics.

[f]*Q* = contrast between subgroups.

[g]$p < .001$.

[h]$p < .05$.

[i]$p < .01$.

Between-Subject Analyses

In the between-subject analyses, only one EMI group per study was included (see 'Coding'). A total of 13 studies were included with 454 participants in the EMI condition and 522 participants in a control condition (waitlist, placebo, or active treatment control). The included studies were not significantly heterogeneous, $Q(12) = 17.17$, $p = .140$. Moreover, the observed true variance was small ($I^2 = 30.13$). A small value of I^2 indicates that a large part of the variance is the result of random error. If one tries to explain this variance (with subgroup analyses), one tries to find an explanation for something that is in essence random [139]. Therefore, no attempt will be made to explain the variance in effect by testing differences due to outcome types and other moderators. Still, a random effect model was adopted because we do not assume a common effect size (despite the lack of statistical significant variance between studies) [139].

The effect for EMI in between-subject studies was $g = 0.40$, 95% CI (0.22, 0.57), $p < .001$ (see Figure 4). This effect can be considered small to medium. The funnel plot (see Figure 5) shows that there is indication for publication bias; the distribution of effects is asymmetrical as the sample size decreases. Specifically, effect sizes are more likely to fall to the right side of the mean when the sample size is small. Furthermore, the Egger's test of intercept is significant, indicating that there is a risk for bias (intercept is 1.50, 95% CI [0.28, 2.72] with $t(11) = 2.71$, one-sided $p = .010$). The trim and fill method was used to account for the missing studies. Six studies were added to the left of the mean (black circles in Figure 5), and the corrected effect size was $g = 0.23$, 95% CI (0.04, 0.42). The corrected effect is considerably smaller than the uncorrected effect, which indicates that the uncorrected effect may be subject to publication bias and needs to be interpreted carefully. On the basis of the standardized residuals, no study was identified as an outlier.

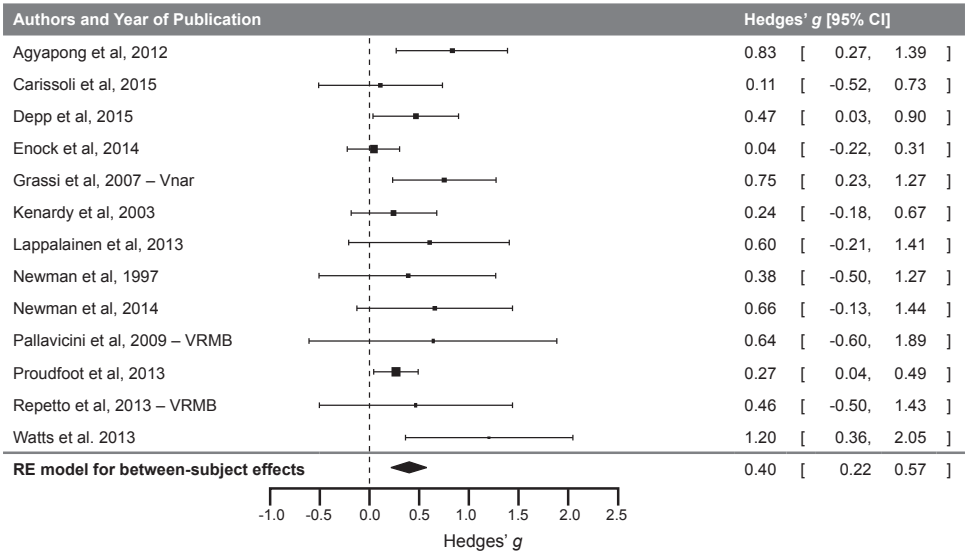

FIGURE 4 Forest plot showing the effect of ecological momentary interventions (EMIs) on mental health complaints for all between-subject studies. The EMI sample (or condition) that was used to represent the active treatment condition is reported after the year of publication

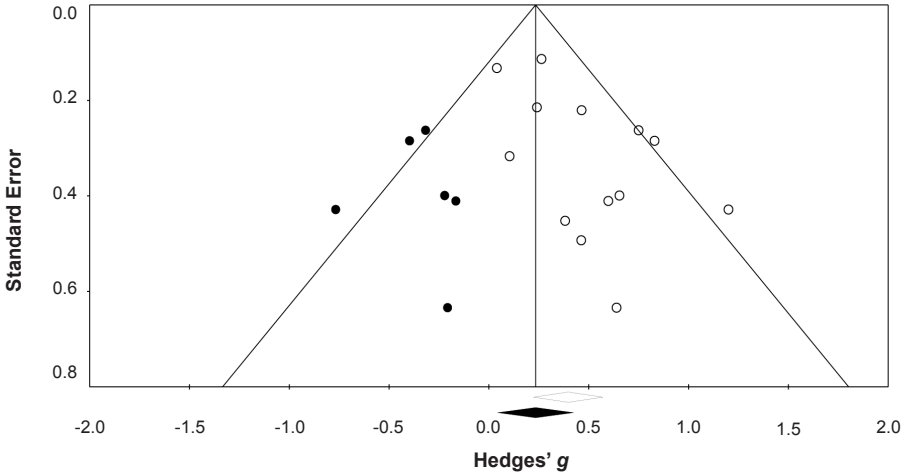

FIGURE 5 Funnel plot of standard error by Hedges' *g* with imputed values based on Duval and Tweedie's trim and fill method (between-subject studies)

DISCUSSION

Principal Findings

The systematic review and meta-analysis was a first attempt to examine whether mobile technologies can be used to provide an effective intervention for mental health and under which circumstances this is the case. A total of 33 studies (n = 1301) were used to answer this question, and the included studies varied considerably in terms of study and intervention characteristics. The quality assessment indicated that the reported study quality was generally low. Specifically, the studies were at risk for bias caused by attrition, reliance on self-report measures, and the failure to blind personnel. Moreover, only a few studies reported using strategies to randomly allocate participants to conditions.

In the within-subject studies (n = 1008), a significant medium effect size (Hedges' g) of 0.58 was found. The estimated effect size did not significantly differ per outcome type (i.e., anxiety, depression, perceived stress, acceptance, relaxation, and quality of life), although no significant effect was found for relaxation. Moderation analysis suggested that the effect on mental health was 62% larger when the EMI was part of a treatment package that included support of an MHP compared with stand-alone EMI. Moreover, this moderation analyses showed that the effect of EMI was smaller, but significant, in the population that had access to care as usual while using the EMI (e.g., inpatient or outpatient setting). It is possible to speculate about what caused this difference in effect; however, a clear comparison of the groups is complicated by the fact that the groups (and included studies) are very diverse. More specifically, the group that received EMIs while also having access to care as usual consisted largely of patients with severe complaints that might be less susceptible to change (e.g., schizophrenia or schizoaffective disorders, borderline personality disorder, and substance abuse).

With regard to the between-subject studies (n = 454), the estimated effect size was 0.40. The effect was, however, subject to publication bias, and the corrected effect was considered small, but significant (g = 0.23).

Both the within- and the between-subject analyses indicate that mobile technologies can be effectively used to deliver interventions for mental health. When interpreting this effect, it must be acknowledged that the effects were considerable smaller in the between-subject studies compared with the within-subject studies. A larger effect in within-subject studies is frequently observed. However, within-subject studies are limited because causality can—generally—not be interfered from these studies. Moreover, these studies have an increased risk for type II errors, which implies

that the conclusions from within-subject studies must be interpreted with caution [176]. Nevertheless, both study types provide a first—and positive—insight into how mobile technology can be used to improve mental health.

The finding that the effect of EMIs was stronger when support by an MHP was included is in line with findings from research on Internet interventions (e.g., [177, 178]). Therefore, although fully automated EMIs can have a positive effect on mental health, it is additionally beneficial to include contact between researcher (or therapist) and participant. This contact could be a helpful tool to increase adherence and motivation, which in turn could result in a stronger effect. Unfortunately, it is currently unknown what levels of support are needed to optimize the effectiveness of EMIs. Future studies should differentiate what kind of contact is necessary for improvement. Not only is it important that we learn how much contact is required, but the *when* (e.g., beginning or during intervention), *how* (e.g., via mobile phone, email, or face-to-face), and *what* (e.g., should support focus on adherence or on the intervention) questions are also worth asking when developing evidence-based interventions [178]. In addition, it is worthwhile to consider which individuals stand to benefit from the support and if support is necessary for everyone. To specify, EMIs can be a valuable (first) step to treat the 'worried well' and individuals with mild symptoms. Using EMIs to treat this group could be economically efficient, as mild problems constitute a major part of all reported mental health problems [179]. Treating this group using the cost-effective EMI methodology, frees resources (such as therapists) for those individuals who are in greater need of more intensive interventions. Moreover, it could help to improve the access to and quality of psychological care. Ideally, the progress of the individuals using the EMIs could be monitored so that alternative intervention options can be recommended when an EMI fails to be effective. Alternative intervention options could entail extra support (while using the EMI), an Internet intervention, or face-to-face intervention. Incorporating EMI in a stepped-care program could help in providing intensive intervention only when needed [180].

Apart from the moderator 'support by an MHP,' no moderation effects were found for the other study or intervention characteristics. The intervention was, for example, equally effective for healthy versus clinical individuals. The absence of significant moderator variables implies that any form of EMI, irrespective of for instance type of training or number of training sessions, is equally effective for all individuals. Obviously, this assumption is implausible, and it is more likely that the null findings are the result of the relative small number of studies that specifically reported the intervention characteristics (e.g., number of training sessions and whether training was triggered) [181]. Considering that the research field of EMIs is relatively new, it is understandable

that limited information is available on what characteristics of an intervention are considered effective (or active). It does, however, highlight the need for research that determines what the active features of an intervention are [182]. Potential questions that could be targeted relate to the frequency and duration of the intervention (e.g., is daily practicing required, and if so, how many times a day?). Although initial research suggests that (daily) repetition is necessary to learn a new behavior [67], this should be further investigated using RCTs with EMIs. Another potential research endeavor is whether a training should be offered on-demand or whether it should be automatically triggered. A meta-analysis, investigating the use of triggers to stimulate engagement with digital interventions, found preliminary support for the use of technology (e.g., text-messages or e-mails) to improve engagement [183]. This result is interesting, as mobile interventions would make it easy to trigger a training, but more studies are needed to establish if this effect is valid. Altogether, it is important that future research focuses on identifying the most potent feature(s) of an intervention.

Limitations

This meta-analysis is limited by the low reported study quality (i.e., 2.29 on a scale from 0 to 6). When the reported study quality is low, the study may be subject to weakness in the experimental setup or to problems in the processing of the data. These shortcomings can influence the true effect and lead to an overrepresentation or underrepresentation [147]. However, reported study quality must not be confused with the actual quality of the study. To explain, studies may have used excellent set-ups but may have failed to adequately report their precise procedure. Indeed, most of the studies failed—on one or more occasions—to provide sufficient information to establish whether there was a risk of bias. To perform correct quality assessments, it is recommended that authors of future studies follow publication guidelines such as the CONSORT statement for RCT [184].

In line with the previous limitation, it is also important that sufficient intervention details are described so that other researchers can fully comprehend what the intervention entailed. In the included studies, the content of the intervention was described, yet other important intervention components—as suggested by Davidson et al. [137]—were not always disclosed. For instance, 10 of the 33 studies (30%) failed to report how the intervention was triggered, and more than half of the studies did not explicate what the compliance with the intervention was. It is imperative that studies describe the full details of used intervention and the compliance with the intervention, and the guidelines by Davidson [137] can be used for this purpose. This information can ultimately be used to determine which interventions (or intervention characteristics)

are the most effective.

Another limitation is that the larger part of the included studies used a within-subject design. Although this design can yield valuable information, RCTs (which use a between-subject design) are considered superior when evaluating interventions because these can be used to establish a causal relation. Moreover, some of the included studies (both within- and between-subject) had small sample sizes. Studies with small sample sizes may be statistically underpowered to detect an effect and have a lower study validity [181, 185]. To further strengthen the body of knowledge on the effectiveness of EMIs, RCTs using adequate numbers of participants are needed.

Conclusions

To conclude, the meta-analysis found a small to medium effect of EMIs on mental health, and this effect did not differ across the different outcome types. Furthermore, the effect appeared to be larger when the EMI was supported by an MHP. It is important that future research determines how support by an MHP can best be implemented and if this support is a necessity for everyone. In addition, new research studies should investigate what the active features of an EMI are. Overall, the use of EMIs for improving mental health is supported; EMIs offer great potential for providing easy and cost-effective strategies to improve mental health and positive psychological well-being in the population.

APPENDIX 1 Specific search strings used to find publications

Search string PsycINFO

(stress* or anxi* or threat* or burden or “self regulation” or nervous* or mood* or depress* or emot* or affect) AND
(“momentary assessment” or “ambulatory assessment” or “personal digital assistant*” or phone* or mobile or mHealth) AND
(“randomized controlled trial” or interven* or “behavior modification” or relaxation* or therapy)

Limits: English | Human | Peer-reviewed
Timespan: All years

Search string Web of Science (Core Collection)

TOPIC: ((stress* or anxi* or threat* or burden or “self regulation” or nervous* or mood* or depress* or emot* or affect)) AND
TOPIC: ((“momentary assessment” or “ambulatory assessment” or “personal digital assistant*” or phone* or mobile or mHealth)) AND
TOPIC: ((“randomized controlled trial” or interven* or “behavior modification” or relaxation* or therapy))

Limits: English
Timespan: All years
Indexes: SCI-Expanded | SSCI | A&HCI

Search string PubMed

Search (stress* or anxi* or threat* or burden or “self regulation” or nervous* or mood* or depress* or emot* or affect) and (“momentary assessment” or “ambulatory assessment” or “personal digital assistant*” or phone* or mobile or mHealth) and (“randomized controlled trial” or interven* or “behavior modification” or relaxation* or therapy)

Limits: English; Humans; Journal Article

Feasibility and effectiveness of a worry-reduction training using the smartphone: A pilot randomized controlled trial

04

Versluis A, Verkuil B, Spinhoven P, Brosschot JF.
British Journal of Guidance and Counselling.
Advance online publication. doi: 10.1080/03069885.2017.1421310

ABSTRACT

Objectives

Worry is an important mediator in the relation between stressors and health. This pilot-study examined whether a smartphone-based in time worry-reduction training was feasible and improved physiological health (i.e., increased heart rate variability [HRV]).

Methods

A total of 26 high-worriers were randomized to an experimental or active control condition (EC and CC respectively). Both conditions registered emotions 5 times daily for a month. The EC additionally received a worry-reduction training with mindfulness exercises. Primary outcomes were feasibility and HRV measured at baseline, after 2 weeks (halfway), and at 4 weeks (post-intervention).

Results

Both training conditions were feasible and well received. HRV increased in the EC and CC, but this increase did not differ between conditions.

Conclusions

Preliminary findings suggest that both training conditions are feasible and might improve HRV, which is an important predictor of cardiovascular disease. This pilot study only provided preliminary evidence, but it laid the groundwork for future randomized controlled trials that ought to include more participants and a waitlist control group in order to get more definitive evidence of the effectiveness of the intervention.

INTRODUCTION

Psychosocial stress, including work stress, is a common phenomenon in industrialized countries [5, 6]. In a large European-wide survey it was for instance found that 22% of the Europeans experience work stress [6]. This is concerning as psychosocial stress is a substantial co-determinant of organic disease, including cardiovascular disease (CVD) (e.g., [22, 23]). There is consensus that the negative effect of stress on health is caused by prolonged physiological activity, like prolonged low levels of heart rate variability (HRV) [10, 25]. HRV refers to the variability in timing between heart beats and low levels of HRV are predictive of CVD [36]. One mechanism that mediates the negative relation between stress and low levels of HRV is worrying [25, 34]. According to the perseverative cognition hypothesis, worrying prolongs the physiological activity caused by stressful events by continuously thinking about these events [25]. In a recent meta-analysis, worry was indeed associated with reduced levels of HRV [34]. In effect, worry prolongs the activation of the stressor in the mind, thereby increasing its negative effect on health. Finding ways to decrease worry might therefore be a good way to reduce physiological activity, which ultimately promotes (cardiovascular) health.

Traditionally psychological interventions take place in a clinical or research setting. A crucial question has been whether new behavior routines, which are adopted in those artificial environments, can be transferred to other contexts (e.g., daily life). Interventions that are given in clinical settings may produce effective skill acquisition when measured in these settings, but the acquired skills may not automatically translate to real life [127]. Neal, Wood, and Quinn [68] argue that this is comprehensible, because environmental cues that were associated with the 'old' behavior may still trigger the occurrence of this behavior. Therefore, training in daily life is considered critical. To translate this to worrying, which can be considered a cognitive coping strategy that people habitually use to deal with stress, it is important to repeatedly train people in their daily lives to cope with their daily stressors in a new way.

A way to train people in their daily lives is by using ecological momentary interventions (EMIs) [71]. EMIs are interventions that are implemented in the daily lives of individuals using a mobile device. A meta-analysis found that EMIs can be effective in improving stress, anxiety, and depression, even when the EMI is not supported by a mental health professional [72]. EMIs can thus greatly reduce therapist time and thereby costs. As mobile phone use is becoming a universal phenomenon, EMIs could be a good way to reach many people. Therefore, the primary focus was to test the feasibility of an in time worry-reduction EMI and to test its effectiveness on reducing physiological activity (which is associated with worry). As primary indicator of

physiological activity, ambulatory measured HRV was used. HRV is typically reduced when people are worrying [34, 42].

The intervention that we pilot-tested was based upon a self-help intervention that has been used by Verkuil, Brosschot, Korrelboom, Reul-Verlaan, and Thayer [87] in a paper-and-pencil format. It requires individuals to recognize when they are worrying and to address these worries in a pre-structured way. Participants are encouraged to reschedule the worry to a later point when no immediate solution to the problem or worry can be thought of. Mindfulness exercises are presented afterwards to stimulate awareness to the present moment [114]. In addition to stimulating awareness of the present moment, these exercises help individuals to become more accepting towards these present moment experiences. Mindfulness-based interventions are considered effective in reducing anxiety and depressive symptoms in both clinical and non-clinical populations (e.g., [115, 186]). Importantly, mindfulness exercises have been previously used as EMI (for a comprehensive overview of EMI studies, including but not limited to mindfulness studies, see [72]). However, few EMIs have been thoroughly investigated using randomized controlled trials (RCTs).

The present study was designed as a pilot study to investigate the feasibility and the preliminary effectiveness of this 4-week in time worry-reduction training with five short training sessions per day. High-worriers were randomized to the experimental condition (EC) or active-control condition (CC; i.e., registering emotions daily). This way, all participants were under the impression that they received a training, but the training in the CC did not include the supposed benefits of the specific therapeutic techniques that were present in the EC (i.e., worry-reduction and mindfulness). Such a CC allowed us to show that secondary effects—like the act of receiving daily prompts to reflect upon ones emotions—were not the main cause of potential benefits. Of primary interest was whether the training was feasible and whether it reduced physiological activity (i.e., increased ambulatory measured HRV). Additional secondary outcomes were included that can be expected to change due to the training. Specifically, heart rate (HR)—as second indicator of physiological activity—and trait and state worry were included. Because mindfulness-based interventions have previously been successful in reducing anxiety, increasing acceptance, and improving affect, these outcomes were also included.

Finally, it was hypothesized that people are not consciously aware of a substantial part of their stress-related cognition while it can still have physiological effects [38, 39]. This so-called unconscious stress can obviously not be directly changed by an intervention. However, there are reasons to expect that a mindfulness training can reduce unconscious stress. The attentional skills that are learned become

automatic, not needing awareness—like with all skill acquisition (e.g., walking, playing the piano) [187]. Unconscious stress was operationalized as implicit affect [38] and was represented as an increase in implicit negative affect and a decrease in positive affect.

Altogether, we expected the EMI (a) to be a feasible intervention and (b) to reduce physiological activity (i.e., increase HRV) compared to merely registering emotions. Secondly, we expected a decrease in HR, worry (both state and trait), and trait anxiety in the EC compared to the CC. Moreover, an increase was expected in acceptance and an improvement in affect (both implicit and explicit) in the EC compared to the CC.

METHOD

Design

A two-arm randomized controlled pilot study was conducted between April and June 2014. Participants were randomized into the EC or CC using a computerized random number generator, which was operated by a researcher who was not involved in the actual data collection. Each generated number was put in a sealed envelope and was disclosed to the research assistant after the participant was included. Participants were unaware to what condition they were allocated. The institutional review board approved of the study protocol (nr. 4689348773). RCTs that followed this pilot were registered in the Dutch trial register (i.e., NTR4827 and NTR4758).

Recruitment

Dutch students were recruited via Leiden University or via acquaintances of the research assistants using advertisements asking for high worrying students who wanted to participate in a worry-reduction training. To determine whether the training can be clinically effective only high-worrying participants were included (i.e., to be able to bring about a reduction in worry complaints). In order to include only high worrying individuals, a cut-off score of 45 or higher on the Penn State Worry Questionnaire was used (PSWQ) [94]. This cut-off can be used as a screening for generalized anxiety disorder, a condition that is fundamentally associated with worry [104]. Participants were excluded if they had a CVD or received psychological treatment during the study period. Twenty-six participants (69% female), with a mean age of 26.35 (SD = 8.69), met the inclusion criteria and agreed to participate.

Outcome Measures

Feasibility. User-experiences were examined using three forced-choice and

four open-ended questions. Three forced-choice questions were answered using a visual analogue scale (VAS) and one using a Likert scale. Example: 'To what extent did the training interfere with your daily activities?' (scored on a VAS ranging from 'not at all' to 'very much') and 'How did you experience the study period?' (scored on a 5-point Likert scale ranging from 'very positive' to 'very negative'). An open-ended example item is 'How many minutes on average did it take you to complete a training session?'

Ambulatory measured cardiac activity. The ECG signal was measured for 24 hr using the ekgMove sensor (Movisens GmbH, Karlsruhe, Germany). This sensor is worn on a chest belt underneath the clothes, thereby making it possible to non-invasively measure ambulatory cardiac activity. The sensor has a resolution of 12 bits, a sampling rate of 1024 Hz, and collects a single channel ECG and data on movement acceleration (using a three-axial acceleration sensor with a sampling rate of 64 Hz). HRV and HR were obtained from the data using Movisens data-analyzer software (Movisens GmbH, Karlsruhe, Germany). The software uses an automated error detection algorithm to process the raw data. The root mean square of successive differences (RMSSD) was used as an index for HRV, as this is the recommended index of HRV in studies using ambulatory assessments [188]. HR was computed in beats per minute (BPM). RMSSD, HR, and movement acceleration were calculated in 30s intervals. Intervals were excluded when HR was below 30 or above 200 BPM (e.g., [189]). Thirty-second intervals were aggregated into hourly averages. Averages were only computed when the hour contained at least 30 min of valid data points. Mean movement acceleration (measured in *g*) was averaged over hourly periods.

Trait and state worry and stressors. The 16-item PSWQ was used to measure trait worry and items were scored on a 5-point scale ranging from 'not at all' to 'very typical.' Higher scores indicate higher levels of trait worry. Cronbach's alpha was good (i.e., between .82 and .92).

State worry and stressors were ambulatory assessed by asking whether the participant had worried and whether a stressful situation had been encountered in the previous period (i.e., in the time period since the last measure) [33]. If participants had worried, they also had to fill in the frequency and the (combined) duration in minutes of the worry episodes. Frequency and duration of state worry were used as dependent variables. When participants had encountered a stressful situation, they had to report the frequency, duration in minutes, and severity of the stressful situation on a 5-point Likert scale ranging from 'not at all severe' to 'very severe.'

Affect. Explicit affect was measured by asking to what extent the participant experienced the four basic emotions. The happiness-score was used as an indication of positive affect and the average of the three negative emotions was used as an index

for negative affect. The dependent variable explicit affect consisted only of the explicit affect questions that were answered during the three test days (scheduled at the start, halfway, and at the end of the training). So, explicit affect questions that were measured as part of the training were not included. Reliability was estimated using the method proposed by Cranford et al. [190]. On the three test days, the between-person reliability was satisfactory (i.e., R_{kf} between 0.98 and 0.99), indicating that the ratings for explicit negative affect were stable and suitable to detect individual differences.

Implicit affect was measured with the Implicit Positive and Negative Affect Test (IPANAT) [191]. The IPANAT presents participants with a nonsense word (e.g., SUKOV) and participants indicate to what extent that word represents the emotion that is jointly presented. Each of the six nonsense-words was coupled with six different emotions (i.e., three positive and three negative). Resulting in 36 pairs and each pair was scored on a 6-point Likert scale ranging from 'doesn't fit at all' to 'fits very well.' To measure implicit affect during the day, each nonsense word was presented at a different moment during the day. The psychometric properties of the IPANAT are satisfactory in student populations [191]. For each test day, reliability coefficients were calculated for implicit positive and negative affect [190]. Implicit affect had adequate between-person reliability (i.e., positive affect: R_{kf} between 0.92 and 0.98; negative affect: between 0.71 and 0.91). So, ratings for implicit affect were stable across each day and reflect individual differences.

Trait anxiety. The 20-item trait-form of the State Trait Anxiety Inventory was used to measure trait anxiety (STAI) [192]. Items were answered on a 4-point Likert scale (i.e., 1= 'almost never', 4 = 'almost always'). Internal consistency was good (i.e., alpha between .92 and .94).

Acceptance. The extent to which individuals accept their negative internal experiences was measured with the 10-item Acceptance and Action Questionnaire-II (AAQ-II; Dutch translation [193]), which was scored on a 7-point Likert scale ranging from 'never true' to 'always true.' Higher scores represent a higher level of acceptance. Internal consistency was good (i.e., alpha between .89 and .91).

Training

The in time training was administered using the Android-based smartphone application MovisensXS (https://xs.movisens.com). The content of the application was specifically developed for research purposes by the first author (AV). Collected data is stored via a wireless Internet connection into a secure electronic environment and can be accessed online. In the application all participants were asked to register the extent to which they experienced the four basic emotions—anger, anxiety, happiness, and sadness—using

a VAS. The CC was told that repeatedly registering emotions was beneficial for health and that this was the training. The EC additionally received a worry-reduction training. This training consisted of answering a series of questions to help individuals focus their attention on the problem that was bothering them at that moment and to constructively think about it (see Figure 1).

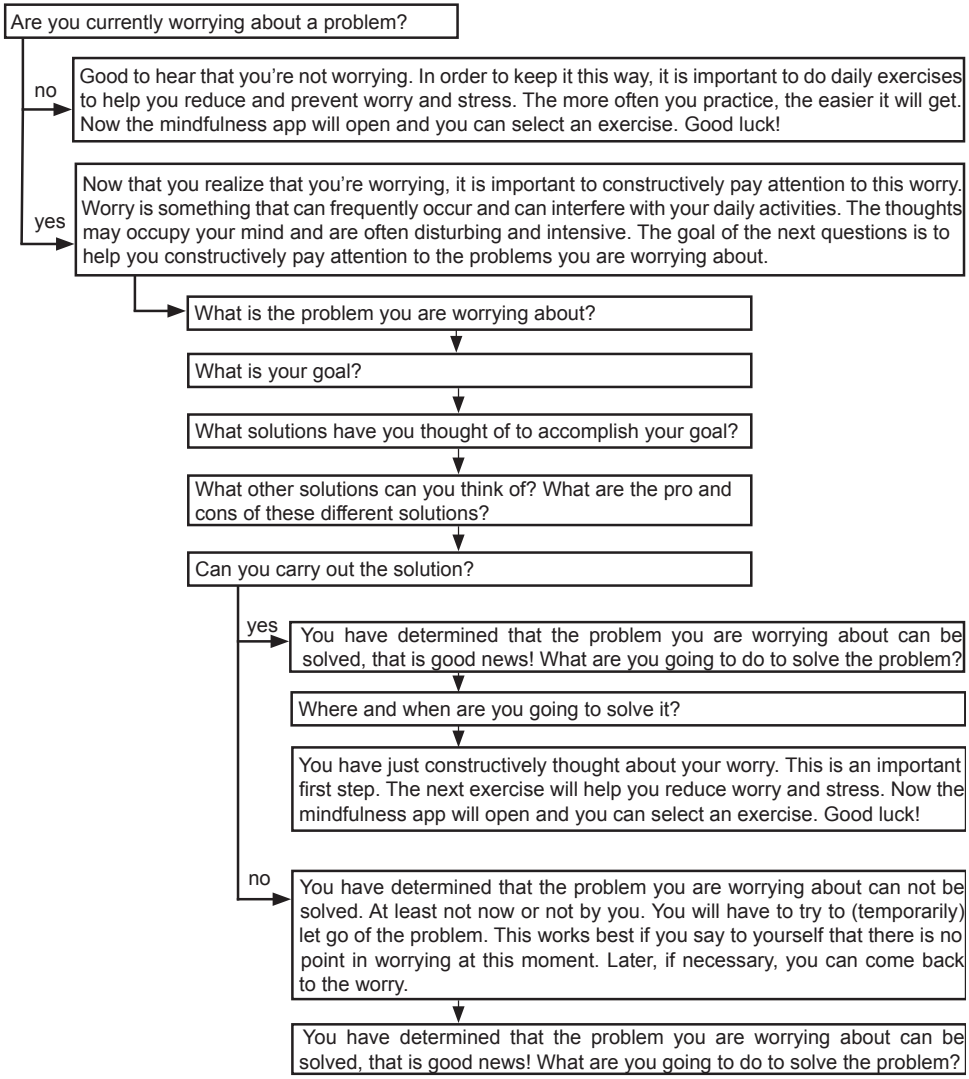

FIGURE 1 Questions as part of the worry-reduction training

Afterwards, they were directed to the application called VGZ mindfulness coach (https://www.vgz.nl/mindfulness-coach-app), which offers 41 mindfulness exercises in audio-format. The exercises cover the central components of traditional mindfulness training; that is, breathing exercises, body scans, and mindful attention exercises [187]. An exercise is automatically selected, however, participants are free to choose another exercise based on their preference or the duration of the exercise (i.e., varies between 1 and 37 min).

Procedure

An online version of the PSWQ was sent to interested individuals to check whether they had sufficient levels of trait worry. If so, participants were contacted and screened for the other exclusion criteria. When a participant met all the inclusion criteria, a lab-meeting was scheduled in which participants were consented and answered demographic questions. Next, participants received information about the study schedule (see Figure 2). Specifically, participants completed three test days that were scheduled before, halfway, and at the end of the training. On these days participants received no training, but completed different assessments. First, cardiac activity was measured by wearing the ekgMove sensor from 11 AM to 11 AM the following day. Second, the questionnaires measuring trait worry, trait anxiety, and trait acceptance were offered online and participants were asked to complete them. Third, the questions measuring state worry, stressors, and implicit and explicit affect were offered on the smartphone and were to be filled in five times during the day.

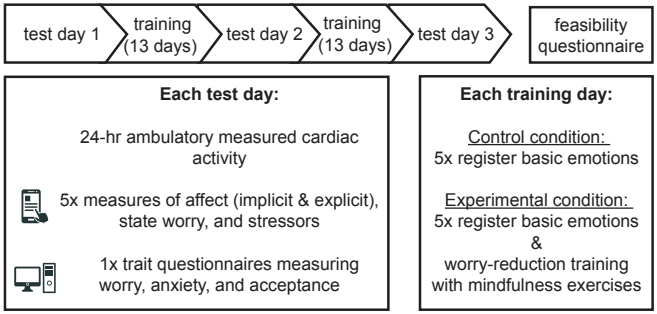

FIGURE 2 Study schedule

The MovisensXS application was used to trigger these questions between 11 AM and 9.30 PM with a minimum of 45 min between triggers. The application also randomly triggered the training sessions, which were offered five times a day between 9 AM and 9 PM on training days (with a minimum of 1 hr between each training session). As

the usual range of triggers is between four and ten per day [71], five was considered acceptable. Participants were motivated to complete as many assessments and training sessions as possible. The triggers could be delayed with 15 min or be dismissed. To stimulate response rates, participants were rewarded 15 Euros when they answered at least 75% of the triggers. Otherwise, they received half this amount. On the last test day participants were informed that they had to fill in the feasibility questionnaire on their smartphone at post-intervention (and no reminder alarm was used).

The necessary applications were installed on their smartphone. A smartphone was lent to participants when they did not own one. Participants were instructed about the correct use of the sensor and before each test day participants were supplied with a charged sensor.

Statistical Analyses

Multilevel modeling was used to analyze whether the different outcome variables changed over time and whether this change differed per condition. For every dependent variable two multilevel models were fitted using the nlme-package in R (version 0.99.484). Model 1 included the predictor time (i.e., 0 = test day 1, 1 = test day 2, 2 = test day 3), thereby making it possible to study how individuals change over time. Model 2 also included the predictors' condition and the Time x Condition interaction, to examine whether the change over time was different between conditions (i.e., 0 = CC and 1 = EC). A continuous time autoregressive structure was used to account for correlation in neighboring measures. Models were fitted using a random intercept and slope, thereby allowing the value of the intercept and slope to vary between participants. Models with convergence problems were simplified by removing the random slope. Assumptions for all models were checked and considered unviolated.

RMSSD and worry duration data were log-transformed, because the raw data was not normally distributed. Untransformed means and standard deviations are reported. Models of the cardiac data were corrected for movement, which accounts for a part of HRV variance.

RESULTS

Descriptive Statistics

The total sample consisted of 26 participants (i.e., n = 11 in EC and n = 15 in CC). Demographic characteristics did not differ between conditions (see Table 1). Four participants dropped out during test day 1. Two participants dropped out due to technical errors and two participants stopped when they became aware that the training

lasted for a month (which they had failed to notice in the initial information). For these participants no physiological data was available. Demographic characteristics did not differ between non-completers and completers (Table 1).

In the final sample, nine participants were in the EC and 13 participants were in the CC. Demographic characteristics did not differ between the conditions (Table 1). Mean RMSSD and HR did differ, respectively $t(19) = -2.18$, $p = .042$ and $t(14.84) = 2.56$, $p = .022$. Participants in the EC had a higher RMSSD and lower HR compared with the CC (see Table 1). Participants completed on average 10.68 (SD = 3.04; 71%) ambulatory assessments and this number did not differ between the conditions ($t(20) = -0.98$, $p = .341$).

TABLE 1 Means (SDs) and percentages of descriptive characteristics at baseline

	Total sample (*N* = 26)	Final sample (*n* = 22)		
Variable	Grouped participants	Grouped participants	Experimental condition (*n* = 9)	Active-control condition (*n* =13)
Gender	69% female	68% female	67% female	69% female
Age	26.35 (8.69)	25.36 (5.22)	25.78 (5.59)	25.08 (5.17)
Stressor frequency	1.37 (0.49)	1.37 (0.49)	1.25 (0.43)	1.44 (0.53)
Stressor duration	34.73 (51.07)	34.73 (51.07)	48.70 (73.86)	26.96 (36.35)
Stressor severity	2.71 (0.82)	2.71 (0.82)	2.80 (0.84)	2.67 (0.87)
State worry - frequency	1.96 (1.05)	1.96 (1.08)	1.87 (1.32)	2.01 (1.02)
State worry - duration	38.63 (53.04)	38.87 (54.90)	36.67 (46.77)	39.98 (60.92)
Trait worry	59.46 (10.12)	58.36 (9.53)	58.67 (9.76)	58.15 (9.77)
Trait anxiety	46.12 (12.04)	45.32 (11.09)	43.33 (9.55)	46.69 (12.22)
Acceptance	41.79 (11.17)	42.50 (10.29)	43.11 (10.61)	42.08 (10.48)
RMSSD		37.39[a] (27.00)	49.75 (36.64)	28.12 (11.42)
Heart rate		83.13[a] (10.59)	77.58 (4.54)	87.29 (12.03)

Note. RMSSD = root mean square of successive differences.

[a]This variable is significantly different between the experimental and control condition.

Primary Outcomes

Feasibility. Eighteen participants (18/22, 82%) completed the feasibility questionnaire (i.e., nine in EC and nine in CC). The VAS's were scored in the expected direction and no significant differences were found between conditions. The easiness with which assessments could be completed on the smartphone was rated between neutral and very easy (M = 66.72, SD = 26.85), and the mean level of interference in

the daily lives that participants experienced due to the training or assessments was scored between 'not at all' and 'neutral' (M = 39.56, SD = 29.02). All participants filled in the assessments seriously, with a score close to 'very serious,' and those in the EC indicated that the mindfulness exercises were completed seriously. The length of an average training session was 2.00 min (SD = 1.50) in the CC and 6.33 min (SD = 2.45) in the EC. This difference was significant, with $t(16) = -4.53$ and $p < .001$. The log-data showed that participants completed on average 3.49 (SD = 0.77) training sessions per day and 94.27 (SD = 21.48) training sessions in total. The number of completed training sessions per day and in total was not different between conditions, resp. $t(20) = -0.74$, $p = .467$ and $t(20) = -.77$, $p = .450$. Lastly, the majority of participants experienced the study period as positive or neutral (i.e., 89%).

Heart rate variability. The preliminary findings showed that RMSSD increased significantly over time for all participants from 37.39 (SD = 27.00) at baseline to 44.26 (SD = 22.42) at post-intervention (with B = 0.04, $p = .005$). The time effect remained when entering condition as predictor (B = 0.05, $p = .009$), but no Time x Condition interaction was observed (B = -0.02, $p = .470$). The magnitude of the change in RMSSD over time, based on the change in RMSSD from pre- to post-intervention, was medium ($d = 0.40$).

Secondary Outcomes

The following outcomes were reported for exploratory purposes and should be interpreted cautiously considering the small sample size. The models for each outcome are reported in Appendix 1. Table 2 displays the means and standard deviations at baseline and at post-intervention, plus the within-subject effect size.

Heart rate. Time was not a significant predictor in model 1 and 2 for average HR. This means that HR did not decrease over time for all participants from baseline to post-intervention, with B = -1.91, $p = .192$ in model 1 and B = -1.32, $p = 0.461$ in model 2. The Time x Condition interaction was also not significant (B = -1.91, $p = .505$). The effect size was negligible ($d = .002$).

Trait and state worry. Model 1 showed that the decrease in trait worry from baseline (M = 58.36, SD = 9.53) to post-intervention (M = 53.09, SD = 13.82) was not significant, with B = -2.70 and $p = .057$. Model 2 showed that the decrease in trait worry was not significantly different between the two conditions, with B = -2.72, $p = .335$, and the effect of time was not significant (B = -1.58, $p = .381$). The reliable change index (RCI) [194], which can produce an unbiased estimate of individual change, showed that two individuals (i.e., one in EC and one in CC) had a reliable change in trait worry from baseline to post-intervention.

For worry frequency and duration no significant main effect of time was found in either model 1 or 2 (i.e., worry frequency: resp. B = 0.14, p = .473 and B = -0.001, p = .998; worry duration: resp. B = 0.10, p = .395 and B = -0.03, p = .816). Moreover, the change over time in worry frequency and duration was not significantly different between the two conditions, respectively B = 0.56, p = .213 and B = 0.26, p = 325).

In terms of effect sizes, the decrease in trait worry from baseline to post-intervention was medium (d = 0.41). The effect size for state worry (both frequency and duration) was between small and medium and in the opposite direction (resp. d = 0.39 and d = 0.33).

Trait anxiety, acceptance, and explicit and implicit affect. None of the predictors in model 1 or 2 were significant for trait anxiety, acceptance, and explicit and implicit positive and negative affect. So, trait anxiety, acceptance, and affect did not change over time and the change over time was not different between the two conditions. The effect size was negligible for trait anxiety (d = 0.05), small and in the expected direction for acceptance (d = 0.24), and mixed for affect. That is, the effect size was negligible for explicit negative affect and implicit positive affect (resp. d = 0.09 and d = 0.06), and was between small and medium—and in the opposite direction—for explicit positive affect and implicit negative affect (resp. d = 0.48 and d = 0.32).

TABLE 2 Means and SDs for all outcome variables at baseline and post-intervention, and the within-subject effect size across all participants

	Baseline		Post-intervention			
Variable	Mean	SD	Mean	SD	*n*	cohen's *d*[a]
RMSSD	37.39	27.00	44.26	22.42	21	0.40
Heart rate	83.13	10.59	83.09	17.16	21	0.002
Trait worry	58.36	9.53	53.09	13.82	22	0.41
State worry - frequency	1.96	1.08	2.44	1.42	12	0.39
State worry - duration	38.87	54.90	39.30	49.00	12	0.33
Trait anxiety	45.32	11.09	44.95	11.29	22	0.05
Acceptance	42.50	10.29	44.27	12.61	22	0.24
Explicit positive affect	62.05	13.87	54.95	21.82	21	0.48
Explicit negative affect	31.03	21.79	29.66	22.50	21	0.09
Implicit positive affect	3.39	0.81	3.33	0.89	22	0.06
Implicit negative affect	2.59	0.56	2.83	0.85	22	0.32

Note. For each outcome a mean and standard deviation (SD) was made using all ratings at baseline and post-intervention; RMSSD = root mean square of successive differences.

[a]Cohen's *d* was used as an estimate of the effect size reflecting pre-post intervention changes.

DISCUSSION

The aim of this pilot study was to investigate the feasibility and preliminary effectiveness of an in time worry-reduction training with mindfulness exercises via a smartphone. Results showed that the implementation of the training was feasible. Specifically, the training (and the assessments) interfered little with the daily lives of participants, were easy to complete, and were taken seriously. On average, more than half of the provided daily training sessions were completed (i.e., 3.5 of the 5 daily sessions; 70%). In all participants a small to medium increase in HRV was observed from baseline to post-intervention. Contrary to our expectation, however, this decrease did not differ between conditions. Moreover, no effects were found for the secondary outcomes. Specifically, no effect was found for HR, worry (both trait and state), trait anxiety, acceptance, and affect (both implicit and explicit). Yet the effect sizes for trait worry and acceptance were small to medium and in the expected direction.

With regard to the primary outcome, our preliminary results suggest that both the in time worry-reduction training with mindfulness exercises and the emotion registration can have a positive effect on HRV, which is an important predictor of CVD. Nevertheless, an increase in HRV was only expected in the condition receiving the worry-reduction training. This is interesting as it implies that merely noticing and registering emotions can have effects on health-related parameters and can thus be seen as an intervention. This is in line with Ockhuijsen, van den Hoogen, Eijkemans, Macklon, and Boivin [195] who found positive effects of emotion registration on anxiety. The experimental set-up does not allow us to test whether emotion registration on itself can be seen as an intervention, as a non-treated waitlist control condition is lacking. Future studies with a waitlist control condition are needed.

On the secondary outcomes no statistically significant results were found. This may suggest that a 4-week worry-reduction training via a smartphone does not improve HR or self-reported psychological parameters. However, results (of both physiological and psychological outcomes) and their statistical significance in a pilot study should be carefully interpreted and cannot be taken as guarantee for treatment success or failure as the sample size is small [196]. Nevertheless, a pilot study is an important first step when developing a novel intervention and can be used to test the feasibility (e.g., [197]). Given that feasibility testing was one of the primary aims of this study, it is surprising or paradoxical that a considerable number of participants failed to complete the feasibility questionnaire (i.e., 4/22, 18%). In other words, the procedure used to complete the feasibility questionnaire was not feasible. The low response rate could be due to forgetfulness, because no alarm was used to notify participants to complete

the questionnaire—thereby allowing participants to complete the questionnaire at a preferred time. Participants were informed—at the start of the last test day—that the questionnaire had to be filled in (and that no alarm was given). Evidently, this procedure was insufficient and in the protocol for the RCT more emphasis should be placed on the necessity to complete the feasibility questionnaire and an alarm could be included as a reminder.

The study did produce useful information about the method to be used to implement an EMI. There was, for instance, no clear guideline on the number of training sessions that is acceptable for individuals. As a result, there is a high variability in the number of training sessions in EMI studies [72]. Based on guidelines for ambulatory assessments, this study incorporated five daily training sessions. The results showed that this is fairly acceptable as 70% of the training sessions were completed and the training sessions did not negatively interfere with participants' daily activities. The study further showed that the randomization procedure worked, that all answers were recorded and stored appropriately, and what kind of technical problems could arise (and how they could be solved). All in all, useful information was gathered that improved the implementation of the following RCTs.

Apart from the fact that this study was a pilot study with a small sample size, a number of limitations can be thought of. First, we did not obtain feasibility data from all participants, which indicates that the feasibility data must be interpreted cautiously. Moreover, no feasibility data was obtained from non-completers. The reasons for dropout could be related to their (potentially negative) experience with the EMI or to other study characteristics. If this were the case, the feasibility may have been presented to optimistically. To learn more about innovation failure, it is important to include dropout participants in the feasibility testing. Nevertheless, this may be difficult as those individuals may not be motivated to complete questionnaires (once they have dropped out).

A second limitation is that we did not have access to log-data of the mindfulness application. Therefore, we were unable to examine variation in the use of the mindfulness exercises. This information could have helped to examine which exercises were used and whether the extent of the practice impacted the results. Ideally, one has this information, but in practice this may not always be feasible when working with commercially available applications (as our mindfulness application).

Another limitation pertains to the randomly triggered training sessions. Using random sampling has advantages, because there is variation in the timing of the training and this increases the generalizability of the trainings effect. However, individuals may not always have access to their smartphones or be able to complete a training session

and this could reduce the number of completed trainings sessions. To account for this, individuals could delay the training for 15 min. Yet 15 min may be too short and studies should consider a longer delay period or personalize the training schedule (to suit an individual).

Despite the mentioned limitations, this pilot study offers an interesting insight; that is, it shows that it is possible to offer a training on a smartphone in daily life (even when there is no contact with a therapist). This is relevant considering that the field of mHealth—which refers to mobile health care—has been expanding and is considered to be the future for delivering (affordable) mental health care [125, 129]. In clinical practice, therapists can use mHealth for different purposes; for instance, (a) to repeatedly assess treatment progress (and this information can be used to inform treatment choices), (b) to deliver homework assignments, psycho-education, or small exercises (like breathing exercises), or (c) to promote adherence by sending motivational or informative phrases (for more details on how mHealth can be used in clinical practice, see [125]).

In conclusion, this pilot study found that a 4-week in time worry-reduction training via a smartphone was feasible. Furthermore, both the group that registered emotion daily and the group that received the worry-reduction training with mindfulness exercises showed an increased HRV. This increase did not differ between the groups. No effects were found on HR or on the psychological outcomes. As small pilot studies are believed to yield biased estimators of effect sizes [197], we believe that it is pivotal to examine the effectiveness of the currently developed, theory-based EMI in a RCT using the active control group as well as a waitlist control group. Still, the EMI methodology has a lot of potential, because it is a cost-effective strategy to reach many people. It can also be used in conjunction with traditional therapy (e.g., to support adherence or to increase therapy effects). Given the high levels of stress in society, it is important that easy interventions are available and smartphones offer great possibilities for this.

APPENDIX 1 Results of primary and secondary outcome variables (n = 22)

	Model 1		Model 2			
	Constant	Time[a]	Constant	Time[a]	Condition[b]	Time x Condition
Multilevel model						
RMSSD[c]	1.61 (0.04)	0.04 (0.01)*	1.57 (0.05)	0.05 (0.02)*	0.10 (0.08)	-0.02 (0.03)
24-hr data	[1.53, 1.69]	[0.01, 0.06]	[1.46, 1.67]	[0.01, 0.08]	[-0.07, 0.28]	[-0.08, 0.04]
Heart rate[c]	74.66 (1.34)	-1.91 (1.46)	76.68 (1.78)	-1.32 (1.79)	-4.38 (2.64)	-1.91 (2.86)
24-hr data	[72.03, 77.29]	[-4.78, 0.96]	[73.18, 80.18]	[-4.83, 2.19]	[-9.84, 1.08]	[-7.52, 3.71]
Trait worry	58.66 (1.95)	-2.70 (1.38) §	59.95 (2.55)	-1.58 (1.79)	-3.22 (4.02)	-2.72 (2.79)
	[54.72, 62.60]	[-5.48, 0.08]	[54.81, 65.09]	[-5.19, 2.02]	[-11.55, 5.10]	[-8.36, 2.92]
State worry - frequency	2.17 (0.36)	0.14 (0.19)	2.34 (0.46)	0.001 (0.22)	-0.58 (0.79)	0.56 (0.44)
	[1.45, 2.90]	[-0.25, 0.52]	[1.41, 3.27]	[-0.44, 0.44]	[-2.27, 1.10]	[-0.33, 1.46]
State worry - duration	2.93 (0.23)	0.10 (0.11)	2.91 (0.28)	0.03 (0.13)	0.01 (0.48)	0.26 (0.26)
	[2.47, 3.38]	[-0.13, 0.33]	[2.34, 3.48]	[-0.23, 0.30]	[-1.01, 1.04]	[-0.26, 0.78]
Trait anxiety	45.96 (2.40)	-0.26 (0.74)	47.88 (3.15)	-0.17 (0.98)	-4.60 (4.89)	-0.21 (1.53)
	[41.11, 50.80]	[-1.74, 1.23]	[41.51, 54.24]	[-2.15, 1.80]	[-14.74, 5.53]	[-3.30, 2.87]
Acceptance	42.09 (2.26)	0.88 (0.79)	40.76 (3.24)	0.12 (1.01)	3.01 (5.03)	2.04 (1.58)
	[37.53, 46.66]	[-0.71, 2.48]	[34.21, 47.31]	[-1.93, 2.17]	[-7.41, 13.44]	[-1.16, 5.24]
Explicit positive affect	61.38 (3.88)	-2.54 (1.59)	59.38 (5.18)	-2.17 (2.12)	4.73 (7.99)	-0.89 (3.22)
	[53.74, 69.03]	[-5.68, 0.59]	[49.17, 69.59]	[-6.35, 2.01]	[-11.85, 21.31]	[-7.23, 5.45]
Explicit negative affect	31.61 (4.42)	-1.33 (1.81)	37.74 (5.62)	-1.78 (2.46)	-14.70 (8.67)	1.12 (3.73)
	[22.90, 40.33]	[-4.89, 2.24]	[26.67, 48.81]	[-6.63, 3.06]	[-32.69, 3.28]	[-6.24, 8.49]
Implicit positive affect	3.47 (0.14)	-0.03 (0.10)	3.69 (0.18)	0.02 (0.13)	-0.53 (0.28) §	-0.12 (0.20)
	[3.19, 3.76]	[-0.22, 0.16]	[3.34, 4.05]	[-0.23, 0.27]	[-1.11, 0.05]	[-0.51, 0.27]
Implicit negative affect	2.65 (0.11)	0.06 (0.08)	2.74 (0.15)	0.02 (0.10)	-0.24 (0.24)	0.13 (0.16)
	[2.42, 2.87]	[-0.09, 0.22]	[2.44, 3.04]	[-0.18, 0.23]	[-0.74, 0.25]	[-0.19, 0.45]

Note. For every predictor the coefficient (standard error) and [95% confidence interval] is reported; RMSSD = root mean square of successive differences.
[a]Time: 0 = first test day, 1 = second test day, and 2 = third test day.

[b]Condition: 0 = control and 1 = experimental.
[c]The models were corrected for movement.
§ = $p < .10$.
* = $p < .01$.

Effectiveness of a smartphone-based worry-reduction training for stress-reduction: A randomized controlled trial

05

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ABSTRACT

Objectives

Perseverative cognition (e.g., worry) and unconscious stress are suggested to be important mediators in the relation between stressors and physiological health. A randomized controlled trial was conducted to examine whether a smartphone-based worry-reduction training improved a physiological marker of stress (i.e., increased heart rate variability [HRV]) and unconscious stress.

Methods

Individuals with high work stress (*n* = 136) were randomized to the experimental, control, or waitlist condition (resp. EC, CC, WL). The EC and CC registered emotions 5 times daily for 4 weeks. The EC additionally received a worry-reduction training with mindfulness exercises. Primary outcome was 24-hr assessments of HRV measured at pre-, mid-, and post-intervention. Secondary outcomes were implicit affect and stress. The effect on heart rate and other psychological outcomes was explored.

Results

A total of 118 participants completed the study. No significant change from pre- to post-intervention was observed for the primary or secondary outcomes. The change over time was not significantly different between conditions.

Conclusions

Findings suggest that the training was not effective for improving HRV or psychological stress. Future studies may focus on alternative smartphone-based stress interventions as stress-levels are high in society, and there is a need for easy interventions and smartphones offer great possibilities for this.

INTRODUCTION

Work stress is known to be a risk factor for the development of decreased mental [198] and physical health, including cardiovascular disease (CVD) [21, 22]. One viable pathway through which (work) stressors exert their unhealthy effects is via prolonged physiological stress responses, including prolonged low levels of heart rate variability (HRV) [10, 25]. According to the perseverative cognition hypothesis, worry is the mechanism that mediates this negative relation between stressors and HRV (e.g., [25, 34]). Interventions that target worries are therefore of interest when aiming to increase HRV, which is an indirect measure of autonomic cardiac control and a marker of CVD risk [36, 199].

Recently the perseverative cognition hypothesis was extended with the hypothesis that a large part of perseverative cognitions are unconscious and that this 'unconscious stress' is also responsible for the prolonged physiological effects of stressors [38, 39]. One could say that worry continues in an unattended fashion. To date no interventions for unconscious stress have been reported. Mental exercises such as cognitive training and meditation, however, have been shown to lead to automatized (i.e., unconscious) cognitive-behavioral changes that are subserved by alterations in the brain—just as with learning skills, like riding a bike [66]. We therefore argue that a brief smartphone-based worry-reduction training, through frequent daily repetition, will lead to automatization of the targeted cognitive changes that will ultimately result in reductions of unconscious stress.

The present study aimed to increase HRV levels and decrease unconscious stress by reducing worry. To do so, we provided people with a worry-reduction intervention in daily life using an ecological momentary intervention (EMI) [72]. EMIs are typically delivered in daily life using a smartphone and this has the advantage of offering the training when people actually experience worry. Moreover, EMIs can be specifically used to provide easy-to-apply and potentially highly cost-effective interventions. Importantly, EMIs have been found to be effective for improving mental health [72]. The stand-alone worry-reduction EMI that was used in the present study consisted of a worry-reduction training [87, 89] and included mindfulness exercises [200]. These short mindfulness exercises were offered to train present moment awareness in daily life. We reasoned that these short, daily mindfulness exercises are easier to implement in the daily lives of individuals than the longer exercises that form part of formal mindfulness-based stress reduction programs. Notably, EMIs with short mindfulness exercises have been found to be effective for improving mental health parameters [72]. Even though the combination of worry-reduction and mindfulness has not been previously studied,

it seems empirically and theoretically plausible to combine cognitive and acceptance-based strategies. To begin with, both strategies are independently associated with decreased worrying [87, 89, 117, 201]. Borkovec et al. [89] suggested that the present moment awareness—that is learned in mindfulness practice—may strengthen the worry-reduction training. Not only is the intervention likely to increase ones attentional control by learning to shift attention from worrisome thoughts to the present moment, but the intervention is also likely to shorten or normalize the experience of stress—and thus the physiological responses—by promoting an accepting attitude towards these present moment experiences. Both the increased attentional control and the reduced stress reactivity are potential pathways through which the intervention may have its effect [202]. By combining a worry-reduction training with mindfulness exercises—thus a strategy focused on change and acceptance respectively—individuals can learn to substitute their habit to worry with a more deliberate and flexible response (for a full rationale on combining cognitive-behavioral treatment strategies with mindfulness, see [203]). Initial evidence suggests that cognitive and acceptance-based strategies can indeed be effectively combined [204, 205]. The EMI was expected to affect HRV via two pathways. First, worry is negatively associated with HRV [34], and reducing worry was therefore expected to increase HRV by shortening the stress response. Second, mindfulness exercises have been shown to increase HRV(e.g., [206, 207]). A pilot study showed that the smartphone-based worry-reduction training with mindfulness exercises is feasible in high-worrying students and is potentially effective for increasing HRV [208]. However, the effectiveness needs to be determined in a larger sample including a waitlist condition.

To this end, a randomized controlled trial (RCT) was conducted. To allow HRV to increase as a result of the EMI, an individuals' level of HRV needs to be low at baseline (because otherwise change is not possible). As physiological screening for study inclusion is laborious, this study recruited individuals based on their level of work stress, because this is negatively associated HRV [209]. Primary aim was to examine the effect of the EMI on HRV assessed for 24 hr at pre-, mid-, and post-intervention. On these days participants also completed assessments of unconscious stress as secondary outcomes.

Testing the effects of the EMI on unconscious stress was important for two reasons. First, not all individuals are able to adequately report their emotional experiences and these individuals are called 'emotionally unaware' [49]. It was hypothesized that not only conscious stress, but also unconscious stress would be associated with low HRV. By measuring unconscious stress, the effectiveness of the EMI on stress could also be determined in individuals who are less aware of their

stress levels [210]. Thus, assessing unconscious stress provided information about the effectiveness of the EMI that was additional to self-reported psychological stress. Second, a reduction in unconscious stress was expected due to the EMI. To explain, the EMI teaches individuals to become aware of experiences and emotions in the present moment. Increasing awareness of emotions is crucial for differentiating between emotions and this is fundamental for emotion regulation [211]. Moreover, the exercises help individuals to be more accepting towards these present-moment experiences. Such an attitude of acceptance can decrease emotional reactivity to stressors and repetitive thoughts [200], and might therefore also be effective for reducing unconscious stress.

Taken together, we expected the EMI to increase HRV and, secondly, to reduce unconscious stress. Additionally, unconscious stress and worry were examined as potential mediators of the effect on HRV. Finally, the effect on heart rate (HR), work stress, anxiety, depression, mindfulness, and explicit affect was explored.

METHOD

Trial Design

A three-arm parallel group RCT was conducted—from September 2014 until June 2016—in Dutch participants who experienced work stress. The study was approved by the institutional review board of Leiden University (nr. CEP 5097802079) and was registered in the Dutch trial register (nr. NTR4758). After the trial was started two changes were made. In August 2015 a change was made to the inclusion criteria (see Eligibility Criteria) and in October 2014 the timing schedule for the measures and training was adjusted. Specifically, the last measure or training was offered at 9:30 PM instead of 10:30 PM.

Participants and Recruitment

A power analysis [212] was conducted to estimate the number of required participants and for the repeated measures analysis a small to medium effect size was used (d = .30). This was based on two previous—related—studies [135, 156] and is in agreement with a meta-analysis that found small to medium effects of EMIs on psychological outcomes [72]. Per condition 31 participants were required with alpha set at .05 and 80% power. To deal with potential dropout we aimed to include 60 participants per condition. Recruitment was stopped before the pre-specified sample size was reached, but the sample size of 136 participants was sufficient based on the power analysis.

Participants were recruited at a healthcare company, by contacting local companies, via advertisements in local and national newspapers, via the newsletter and

website of Leiden University, and by mention on the local and national radio. Interested individuals were directed to the website http://www.piekeren.com for information. Individuals could complete the initial screening questionnaire on the website. A total of 588 participants completed the questionnaire; 74% was female with a mean age of 43.60 (SD = 11.39).

Eligibility Criteria

Participants were included if they were: (a) 18 years or older, (b) employed, (c) competent in using a smartphone, and (d) experienced work stress thereby making it a clinically relevant sample. Work stress was operationalized as an imbalance between effort and reward (i.e., high effort and low rewards), and was measured using the Effort-Reward Imbalance questionnaire (ERI) [213]. An ERI index of greater than 1.00 was chosen as cut-off score since it is associated with adverse health effects (e.g., [209, 214]). During the study the ERI criterion was lowered to 0.89 to increase the influx of new participants. The new ERI criterion was based on the 216 individuals who had completed the screening questionnaire up until August 2015 and the criterion was set 20% below the median of this group.

Individuals were excluded when they: (a) were receiving treatment for psychological or psychiatric problems, (b) had or have had a CVD, (c) used medication that can influence cardiac activity, (d) abused substances, (e) had a history of or current severe psychological disorder (e.g., schizophrenia), and (f) had a latex allergy (i.e., participants had to wear a HR monitor which contained latex). Additionally, (g) individuals who reported suicidal ideation in the past 2 weeks were excluded and referred to their general practitioner for counseling.

Randomization

Eligible participants were randomized into the EC, CC, or WL using a random number generator (https://www.random.org). Each number referred to a study condition and was put in a sealed envelope by a research assistant not involved in the data collection. Once a participant was included in the study, the allocated condition was disclosed to the researcher. On day 1 of the study, participants were told whether they were allocated to a training or WL condition.

Training

The smartphone application MovisensXS (https://xs.movisens.com) was used to offer the training in the CC and EC. During each training session, all CC and EC participants had to rate their emotions on a visual analogue scale (VAS) ranging from ‘not at all’ to

'very much' (i.e., 'To what extent are you experiencing happiness, anger, sadness, and anxiety?'). The CC was told that the training consisted of simply registering emotions and that this can increase the ability to recognize and describe emotions, which in turn is important for reducing stress. After emotion registration, the EC received a worry-reduction training in which a series of questions were presented (see, [208]). The aim was to help individuals recognize when they were worrying and to address these worries in a pre-structured way [87]. Next, participants completed a mindfulness exercise using the VGZ mindfulness coach application (https://www.vgz.nl/mindfulness-coach-app). The application automatically selected an exercise, but participants were free to select a specific exercise based on, for instance, their preference (i.e., from 41 different audio-based exercises varying in length from 1 to 37 min). The application contains (a) breathing exercises that encourage a slow and deliberate breathing, (b) body scans to help individuals focus their attention on the bodily sensations whilst keeping an accepting attitude towards these experiences, and (c) mindful-attention exercises to increase moment-to-moment experiences, for instance, by focusing on the direct environment. The application was previously found to be effective for increasing mindfulness and decreasing general psychiatric complaints [215].

Primary Outcome Measure

Ambulatory assessed cardiac activity. The ekgMove sensor (Movisens GmbH, Karlsruhe, Germany), which is worn on a chest belt underneath the clothes, measured cardiac activity continuously on the three test days. The sensor collected single channel ECG data with a resolution of 12 bits and a sampling rate of 1024 Hz. The sensor recorded movement acceleration data in *g*. The sensors' accuracy in detecting R-peaks—based on the sensor sensitivity and positive predictive value—was comparable to a medical standard measurement system [216]. Movisens data-analyzer software processed the raw data using an automated error detection algorithm to clean the ECG signal from artifacts. HRV and HR in beats per minute (BPM) were calculated using the cleaned ECG signal. As an index of HRV, the root mean square of successive differences (RMSSD) was used [35]. This HRV index is recommended in ambulatory assessment studies [188]. RMSSD, HR, and movement acceleration were calculated in 30 s intervals. Intervals were excluded when HR was below 30 or above 200 BPM (e.g., [189]), or when artifacts had been detected within that interval. The remaining intervals were aggregated into hourly averages, but only for hours that consisted of at least 30 min of reliable data.

Secondary Outcome Measures

Unconscious stress. Unconscious stress was operationalized as implicit affect (i.e., increased implicit negative and decreased implicit positive affect) and as increased implicit stress measured with the stress Implicit Association Test (IAT) [217].

Implicit affect. The Implicit Positive and Negative Affect Test (IPANAT) [191] measured implicit affect. The IPANAT presented six nonsense words (e.g., RONPE) and each word was presented with an emotional adjective. Participant indicated on a 6-point scale ranging from 'doesn't fit at all' to 'fits very well' to what extent the nonsense word represented the emotion. Each nonsense word was coupled with three positive emotions (e.g., happiness) and three negative emotions (e.g., tense). The tendency of participants to rate the nonsense words as sounding positive or negative determines the level of implicit positive and negative affect respectively. Positive and negative affect were considered implicit, because participants were unaware of the construct that was measured [191]. The IPANAT was adjusted for ambulatory assessment. Specifically, each nonsense word was presented at a different time during the day [218]. Internal consistency, test-retest reliability, and construct and criterion based validity were adequate among students [191]. The between-person reliability coefficients per test day were good for both implicit negative and positive affect (i.e., R_{kf} .91 or higher), which means that the ratings reflect individual differences and are stable across test days [190].

Implicit stress. The IAT was adapted to measure implicit stress. The IAT is a computer task with five blocks. In each block participants are presented with words that have to be categorized—as fast as possible—into their corresponding categories using a corresponding key. Block 3 and 5 are the critical blocks and consisted of 20 practice and 60 actual trials. In these blocks participants were shown five self-related words, five other-related words, five stress-related words, and five relaxed-related words (see Appendix 1). One word was presented at a time and the category labels—into which the words had to be categorized—were displayed at the top left and right side of the screen. In block 3 the words *self* and *stress* were displayed on the left, and the words *other* and *relaxed* are displayed on the right side of the screen. In block 5 the *self* and *other* labels switched sides. A scoring algorithm was used to calculate an IAT score, with higher scores reflecting higher levels of implicit stress [219]. The IAT has acceptable internal consistency, test-retest reliability, and predictive validity [220, 221].

Work stress. The 22-item ERI assessed work-related effort, reward, and overcommitment. An ERI index—as indication of work stress—was computed by dividing the effort by the reward score, whereby the latter was corrected to account for the unequal number of items. Psychometric properties were satisfactory [213] and

Cronbach's alpha of the scales ranged from .67 to .81 in this study.

Trait worry. The 16-item Penn State Worry Questionnaire (PSWQ) [94] measured trait worry. Internal consistency, test-retest reliability, and predictive validity are considered good [94, 95, 222]. Cronbach's alpha ranged from .89 to .91.

State worry and stressors. Using ambulatory assessments, participants were asked whether they had worried and if they had experienced a stressful situation since the last measure. This specific instruction was used in previous research (e.g., [218]). If a positive response was given, participants also indicated the frequency, duration, and severity of those episodes on 5-point scale ranging from 'not at all severe' to 'very severe.' Frequency, duration, and severity of state worry were used as dependent variables.

Anxiety and depression. The 7-item Generalized Anxiety Disorder scale (GAD-7) [223] and the 9-item Patient Health Questionnaire (PHQ-9) [224] measured respectively self-reported anxiety and depression in the past 2 weeks. The questionnaires have good internal consistency and validity in both the clinical and the general population [225]. In the present study Cronbach's alpha ranged from .78 to .83 for anxiety and from .67 to .75 for depression.

Mindfulness. The 39-item Five Facet Mindfulness Questionnaire (FFMQ) [226] assessed the tendency of individuals to be mindful in their daily lives. The sum of all items was used as the outcome variable. Psychometric properties are acceptable in the general population and in meditating samples [226, 227]. Cronbach's alpha ranged from .85 to .90.

Explicit affect. Using ambulatory assessments, participants indicated to what extent they experienced the four basic emotions on a scale from 'not at all' to 'very much.' Anger, anxiety, and sadness were averaged to represent negative affect, and the happiness-rating represented positive affect. Affect measured on the test days was used as dependent variable. Between-person reliability, per test day [190], was good (i.e., R_{kf} .96 or higher). Indicating that ratings were stable across test days and capable of detecting individual differences.

Treatment credibility. The 6-item Credibility / Expectancy Questionnaire (CEQ) [228] examined treatment expectancy and credibility of the treatment rationale. Internal consistency and test-retest reliability are considered good [228]. Cronbach's alpha was .77 for the credibility scale and .51 for the expectancy scale. Considering the low internal consistency of the expectancy scale, we used a single item to represent expectancy (i.e., 'By the end of the therapy period, how much improvement in your symptoms do you think will occur?').

Feasibility. Study feasibility was defined as the experience of participants

with the study period and with the training. It was examined at post-intervention using forced-choice and open-ended questions that were answered on a smartphone.

Procedure

Interested individuals completed an online screening questionnaire that checked the majority of the inclusion and exclusion criteria, and contact information was obtained. Ineligible individuals were notified and eligible participants were called by phone to check for latex allergy, medication use, suicidal ideation, and whether the individual was currently receiving psychological treatment. Eligible individuals were explained that the study lasted 4 weeks and that an appointment was scheduled at the start, halfway, and on the final day of the 4 weeks. Each appointment was scheduled on a weekday before 11:00 AM and the researcher traveled to the participant for the appointment. The appointment days were called test days, because on these days participants completed different assessments and no training was scheduled. When participants did not own a smartphone or when the operating system of a participants smartphone was not Android or IOS, a smartphone was lend to the participant.

During the first appointment participants were consented, asked to complete a demographic questionnaire, and informed whether they were allocated to a training-condition (i.e., CC or EC) or to the WL (i.e., only assessments on the three test days). Details about the scheduled assessments were provided (see Figure 1).

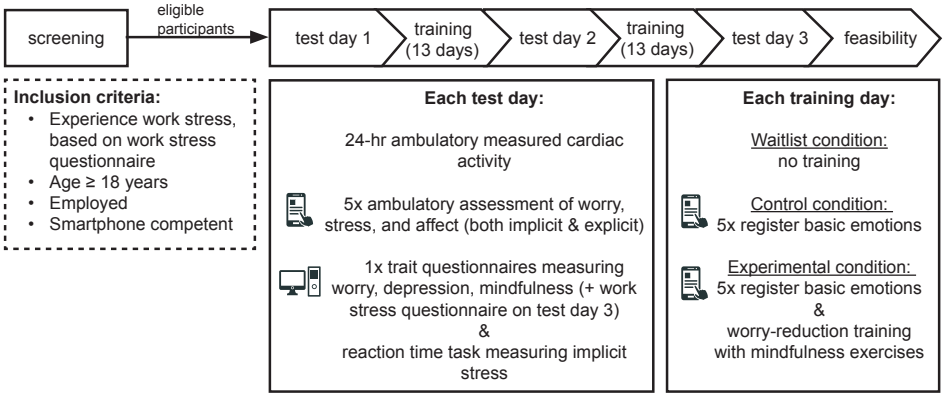

FIGURE 1 Study overview

First, ambulatory cardiac activity was assessed continuously for 24 hr from 11:00 AM onward. Second, trait questionnaires and the task assessing implicit stress were completed online. Third, ambulatory assessments of state worry, stress, and affect

were scheduled five times during each test day—randomly between 11:00 AM and 9:30 PM—with 75 min between assessments. Assessments were triggered using the smartphone application MovisensXS. In between the test days, in the CC and EC, five training sessions were randomly triggered between 9:00 AM and 9:30 PM with at least 90 min between sessions. Triggers could be delayed for 30 min or dismissed. Participants were entered into a lottery to win prizes (e.g., tablet) when they answered at least 75% of the triggers, thereby stimulating full and complete participation. Their chance of winning increased when they answered more triggers. The CC and EC additionally completed the Credibility / Expectancy Questionnaire. At the end of the first appointment the smartphone applications were installed. Participants received a booklet with study procedure information and a fully charged sensor to measure cardiac activity. During the second and third appointment participants were reminded which assessments took place and a charged sensor was provided. On the final test day participants were reminded to complete the feasibility questionnaire on their smartphone at post-intervention.

Statistical Analyses

Multilevel modeling was used to examine the effect of the intervention on RMSSD, unconscious stress, HR, work stress, trait worry, worry severity, anxiety, depression, mindfulness, and explicit affect. Using the nlme-package in R (version 3.0.3) two models were fitted per outcome variable. Model 1 examined how individuals changed over time by including the predictor time (i.e., 0 = test day 1, 1 = test day 2, 2 = test day 3). Model 2 examined whether the change over time was significantly different between conditions by additionally including the predictor condition (i.e., 0 = WL, 1 = CC, 2 = EC) and the Time x Condition interaction. A random intercept and slope was included in all models, and a continuous time autoregressive structure was used to account for autocorrelation. In case of convergence problems, the random slope was removed to reduce the models' complexity. All the models that included a cardiac outcome were corrected for movement acceleration as it naturally accounts for a part of the variance in HRV.

The count variables (state) worry frequency and duration were analyzed using generalized linear mixed models. To allow for overdispersion, a negative binomial distribution was used. In line with the above-described analyses, two models were fitted: model 1 included the predictor time and model 2 included the predictor time, condition, and Time x Condition interaction.

To examine whether the change in the primary outcome variable RMSSD was mediated by worry or unconscious stress, mediation analyses were done when

relevant based on the results of the multilevel models [229]. That is, when there was a significant association between (a) predictor (i.e., condition) and outcome variable, (b) predictor and mediator, and (c) mediator and outcome variable.

We additionally checked for group differences at baseline, examined whether study attrition was different across conditions and was related to age, gender, or level of work stress. Further, study and training acceptability, and training adherence was compared across conditions. A reliable change index (RCI) [194] was calculated for an outcome variable when a significant change from pre- to post-intervention was found, and the RCI estimates how many participants showed a reliable change.

Work stress and the RMSSD data were not normally distributed and were therefore log-transformed. In the Results, the untransformed means and standard deviations are reported. An IPANAT response was excluded from the analyses when each emotional adjective that was coupled to a nonsense word—so both positive and negative emotional adjectives—was scored identical (e.g., 2-2-2-2-2-2) as this indicates false responding.

RESULTS

Descriptive Statistics

Hundred and thirty-six participants were included and randomized across conditions (see Figure 2). Table 1 displays the descriptive statistics of the excluded and included participants. The groups did not differ on age, gender, or on whether they had experienced psychological complaints in the past. Compared to excluded participants, included participants had higher levels of work stress ($t(402.41) = -3.93$, $p < .001$). Eight participants dropped out before the start of the study, resulting in a final sample size of 128 participants. Dropout prior to the first test day was not related to condition.

In the final sample, the baseline level of trait worry was high [104]. Moreover, depression and anxiety were mild [223, 224], and both correlated positively with implicit stress (resp. $r = .21$, $p = .018$ and $r = .26$, $p = .004$). The baseline clinical characteristics were for the most part similar across conditions. Only implicit positive and negative affect differed significantly, with $F(2,121) = 10.96$, $p < .001$, $\eta_p^2 = .15$ and $F(2,121) = 5.18$, $p = .007$, $\eta_p^2 = .08$. Specifically, the EC had higher implicit negative affect compared to the WL, and had higher implicit positive affect compared to both the WL and CC (resp. $p = .005$, $p = .007$ and $p < .001$). The means and standard deviations of the primary and secondary outcome variables are reported in Table 2. The other outcome variables are reported in Appendix 2.

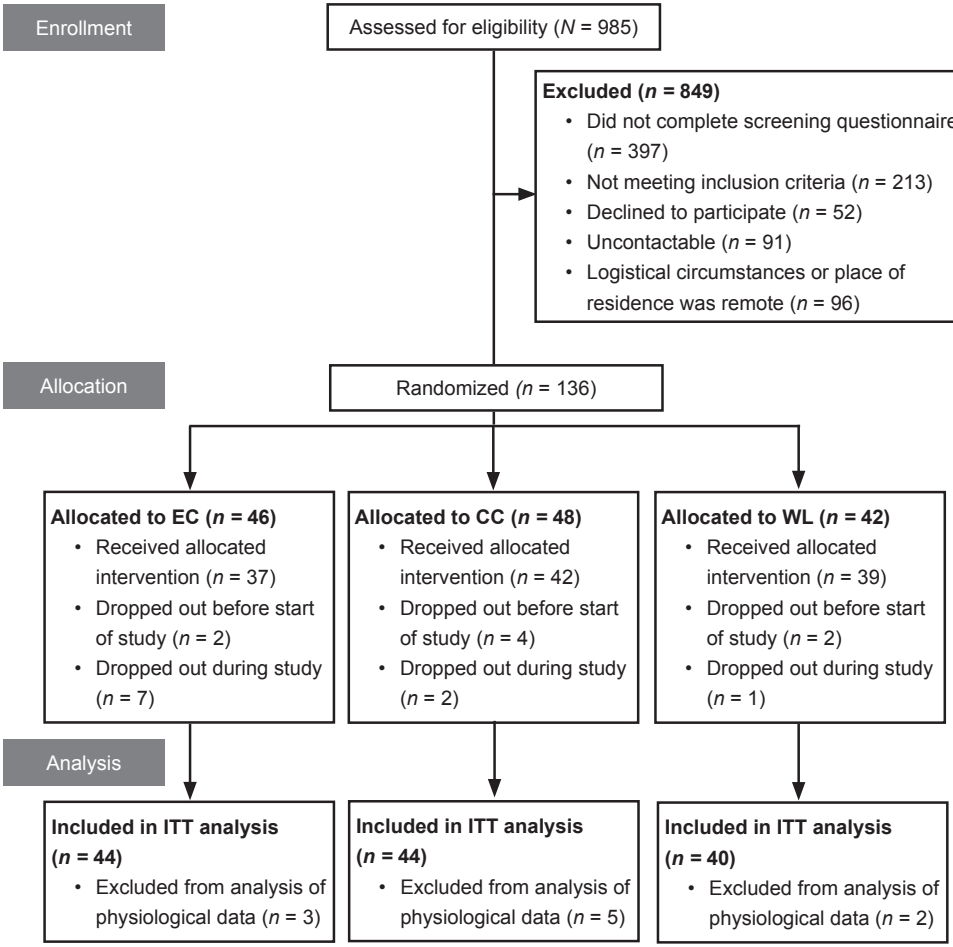

FIGURE 2 Flow diagram

Even though we screened for medication use, ten participants used medication during the study that can influence cardiac activity (e.g., temazepam). Therefore this physiological data was excluded, although the results did not change as a result of their exclusion. So, physiological data of 118 participants was analyzed. Cardiovascular activity at baseline was comparable across conditions and values were within the normal range [35, 199]. Moreover, the average baseline level of RMSSD was comparable to the averages of other populations who experienced work stress [209]. Baseline RMSSD and HR were not associated with work stress (resp. $r = .07$, $p = .573$ and $r = .17$, $p = .144$).

At post-intervention, the attrition rate was 8% (10/128). A Fisher's exact test indicated that attrition during the study was more likely in the EC compared to the

grouped CC and WL condition (p = .031, ϕ = .22). Gender and age were not related to attrition, but dropout participants had higher baseline levels of work stress (M = 1.37, SD =0.36) compared to study completers (M = 1.16, SD = 0.17) with t(126) = -3.01, p = .003.

At pre-intervention, the average credibility and expectancy of the training did not differ between the EC and CC. Participants in both conditions reported a medium credibility (M = 6.90, SD = 1.05; scale from 1 - 9) and moderate expectations (M = 57%, SD = 18.73).

TABLE 1 Means (SDs) and percentages of demographic and clinical characteristics of the included and excluded participants at baseline

	Excluded sample (n = 452)	Included sample (n = 136)
Demographic variables		
Gender	75% female	71% female
Age	43.71 (11.39)	43.23 (11.39)
Nationality (% Dutch nationalities)	—	95%
Education level (% completed first stage of tertiary education)	—	70%
Clinical characteristics		
Work stress	1.08 (0.35)	1.18 (0.20)
Psychological complaints: past[a]	48%	46%
Psychological complaints: current[a]	29%	14%
Psychological complaints: treatment[a]	27%	0%

[a] Indicated with the percentage of positive responses.

Training Adherence and Acceptability

The mean number of completed training sessions per day was significantly higher in the CC compared to the EC, with t(60.42) = 2.62 and p = .011.The CC completed on average 75% of the daily training sessions (3.74/5, SD = 0.76) and the EC completed on average 63% of the daily training sessions (3.15/5, SD = 1.18). Training frequency was unrelated to gender, age, or baseline levels of work stress.

Considering the importance of daily practice, adherence was operationalized as completing at least one training session on each of the 26 training days. A total of 46 participants in the EC and CC adhered (i.e., 58% of the 79 participants). In the CC, 74% (i.e., 31/42) achieved complete adherence compared to 41% (i.e., 15/37) in the EC. This difference was significant (t(72.84) = 3.11, p = .003).

At post-intervention, 101 participants (i.e., 32 in EC, 36 in CC, and 33 in WL) completed the feasibility questionnaire. In general, participants experienced the study

period between neutral and very positive (M = 66.62, SD = 14.07), found it relatively easy to complete the assessments and the training on the smartphone (M = 73.19, SD = 23.71; VAS ranging from 0 to 100), and completed the ambulatory assessments seriously (M = 82.09, SD = 14.24; VAS ranging from 0 to 100). There was no significant difference between conditions. The level of interference that participants experienced in their daily lives due to the training or assessments did differ between conditions ($F(2,99) = 17.38$, $p < .001$, $\eta_p^2 = .26$). The EC experienced higher levels of interference compared to both the CC and WL ($p < .001$). Specifically, the CC and WL scored the level of interference between 'not at all' and 'neutral' (resp. M = 30.04, SD = 19.17 and M = 28.54, SD = 25.25), whilst the EC scored close to 'neutral' (M = 56.47, SD = 19.84; on a VAS ranging from 0 ['not at all'] to 100 ['very much']). Additionally, the extent in which the participants believed that the training had helped them to 'deal with stress' was scored around neutral in the EC and CC (M = 47.36, SD = 21.20; VAS ranging from 0 to 100), and did not differ significantly between conditions ($t(63) = -1.91$, $p = .061$). The training duration was significantly higher in the EC compared to the CC, with $t(65) = -3.16$, $p = .002$. On average, the duration was 3 min and 53 s (SD = 3.95) in the CC and 7 min (SD = 4.51) in the EC. The EC and CC reported that they completed the training sessions seriously, with a score between 'neutral' and 'very serious' (resp. M = 69.00, SD = 16.66 and M = 84.28, SD = 14.67). The difference between the EC and CC was significant, with $t(64) = 3.96$, $p < .001$.

Primary Outcome Measure

RMSSD did not significantly change from pre- to post-intervention in model 1 or 2 (resp. B = -0.02, $p = .507$ and B = -0.05, $p = .206$) and the change over time was not significantly different between conditions (B = 0.03, $p = .251$). The models—and the models for the secondary outcomes—are reported in Appendix 3. The average amount of movement remained constant over time and did not differ between the conditions.

Secondary Outcome Measures

No significant Time x Condition interactions were found for unconscious stress (i.e., both implicit affect and implicit stress). Indicating that the change over time was not significantly different between conditions. Implicit stress did decrease over time for all participants in model 1 (B = -0.04, $p = .019$), with four participants showing a reliable change (↓= 3 in EC; ↑= 1 in EC).

Furthermore, the effect of the intervention on HR, work stress, worry (both trait and state), anxiety, depression, and mindfulness was explored. As the analyses are exploratory, no corrections were employed for multiple testing. Again, no significant

Time x Condition interactions were found. Several main effects of time were found across all participants. Specifically, trait worry decreased over time in both model 1 and 2 (resp. B = -1.36, $p < .001$ and B = -1.18, $p = .014$). State worry severity and mindfulness increased over time in model 1 (resp. B = 0.18, $p = .001$ and B = 1.47, $p = .016$), but not in model 2 when condition was accounted for. Eleven participants had a reliable change in trait worry (↓= 7 in EC, 1 in CC, 3 in WL), four participants had a reliable change in state worry severity (↓= 1 in EC; ↑= 2 in EC, 1 in WL), and eight participants had a reliable change in mindfulness (↓=1 in EC, 1 in CC; ↑= 4 in EC, 3 in CC, 1 in WL).

TABLE 2 Means (SDs) of primary and secondary outcome variables at pre-, mid-, and post-intervention for each condition

	Experimental condition	Control condition	Waitlist condition
***n* at each time point**			
Pre-intervention[a]	44 | 41	44 | 39	40 | 38
Mid-intervention[a]	37 | 34	42 | 37	39 | 35
Post-intervention[a]	37 | 34	42 | 34	39 | 37
Outcome variables	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
RMSSD			
Pre-intervention	37.17 (20.01)	40.46 (23.48)	41.84 (19.50)
Mid-intervention	39.54 (18.94)	39.74 (19.90)	49.20 (28.66)
Post-intervention	42.97 (24.55)	37.56 (22.91)	44.83 (28.67)
Implicit negative affect			
Pre-intervention	1.52 (0.78)	1.25 (0.61)	1.03 (0.59)
Mid-intervention	1.83 (0.77)	1.44 (0.73)	1.09 (0.78)
Post-intervention	1.54 (0.75)	1.24 (0.63)	1.01 (0.65)
Implicit positive affect			
Pre-intervention	2.19 (0.88)	1.46 (0.69)	1.68 (0.60)
Mid-intervention	2.16 (0.77)	1.23 (0.75)	1.61 (0.76)
Post-intervention	2.34 (0.68)	1.64 (0.78)	1.75 (0.71)
Implicit stress			
Pre-intervention	-0.41 (0.33)	-0.38 (0.28)	-0.39 (.0.38)
Mid-intervention	-0.51 (0.35)	-0.34 (0.33)	-0.47 (0.24)
Post-intervention	-0.49 (0.28)	-0.42 (0.30)	-0.50 (0.23)

Note. RMSSD = root mean square of successive differences.

[a]The first sample size reflects the number of participants that was available for analyses of the psychological outcomes and the second sample size reflects the number of participants that was available for the physiological data analysis.

Mediators of Treatment Effect

No mediation analyses were performed, because the change in RMSSD was not predicted by condition and that was the first requirement.

DISCUSSION

This RCT investigated whether a worry-reduction EMI with mindfulness exercises could be used to increase HRV and unconscious stress in individuals with high levels of work stress. No change over time was found on the primary outcome HRV. Furthermore, the change over time was not different between conditions and therefore we were unable to test whether changes in HRV were mediated by trait worry or unconscious stress. Likewise, no differential effects were found for the secondary outcome unconscious stress or for any of the other outcome variables.

A decrease over time in implicit stress and trait worry and an increase in state worry severity and mindfulness was found for all participants. Yet after controlling for condition, only the time effect for trait worry remained with the majority of reliable change occurring in the EC (7/11, 64%). Even though a decrease in trait worry can be expected in the EC, this finding is somewhat remarkable for participants in the WL condition (3/11, 27%). The time effect is therefore more likely the result of a phenomenon called measurement reactivity, whereby self-monitoring of a behavior at time one can alter monitoring of that behavior at time two [103].

Contrary to our expectation, the findings suggest that the EMI was not effective for improving HRV or unconscious stress. This may be explained by the fact that the proposed mediators worry and unconscious stress did not decrease as a result of the intervention. Nor did mindfulness increase in the EC. Both of these findings suggest that the EMI was not successful in its current format.

The intervention may have been ineffective, because the length of the actual training sessions was too short to accomplish change (i.e., average duration was 7 min in the EC). However, exploratory results—which are not reported—suggest that the duration of the mindfulness exercises was not a moderator of effect, nor was the total number of training sessions, the mean number of daily training sessions, or the level of initial work stress. Instead of increasing the length of the training sessions, future studies could individualize the exact dosage of the intervention, because learning a new skill may take variable amounts of time in practice among individuals. Future studies should also consider incorporating support from a mental health professional into the EMI protocol as this additional support can increase the effectiveness of EMIs [72].

A second potential reason for the inefficacy of the EMI is the adherence to

the training frequency. Notably, daily practice was considered important, yet only 41% of participants in the EC adhered to at least one training session per day. This could suggest that some participants were unmotivated and/or were unable to complete a stand-alone intervention without additional support. It could also indicate that the EMI was not well suited for the current population. To illustrate, these stressed individuals received a training also during work hours. These individuals, however, already perceive work demands that exceed their coping capacities. Adding the training—during work hours—might actually have the opposite effect and increase their level of experienced stress. This calls for careful consideration of EMI characteristics that relate to the implementation of the EMI into the daily life of individuals.

Another reason for the inefficacy of the EMI could be specifically related to the way in which mindfulness skills were trained. Participants were free to choose which mindfulness exercise they wanted to do. This could have been problematic, as it may have offered too much variability in both the type and duration of the exercises. Perhaps a more structured intervention is necessary that specifies which exercise of what length should be done at what time. Even though the intervention would lose its flexibility, it may be necessary to first train foundational mindfulness skills using more prolonged exercises. Potentially more flexibility in the intervention could be integrated at a later stage.

Regarding the generalizability of the findings this study used a new combination of interventions (i.e., worry-reduction with mindfulness exercises) and a new delivery method (i.e., EMI). Our null results do not rule out the possibility that other self-contained worry-reduction or mindfulness interventions are effective, although the literature seems to favor a combination of the two strategies. It is also possible that the combination of the interventions that we used is actually effective, but not when provided as an EMI. Given the exponential rise in EMIs, future studies are needed to determine whether different combinations of worry-reduction strategies with mindfulness are useful and what platform can best be used to implement the training.

Several other limitations need to be considered when interpreting the results. First, participants were recruited based on their level of work stress, which was expected to be associated with HRV. In contrast to previous studies [209], the results showed that high work stress was not associated with lower HRV. This indicates that screening for low HRV, using the work stress questionnaire, might not be a good substitute for physiological screening and future studies should consider incorporating physiological screening into their study protocol. The absence of an association between work stress and HRV might also be the result of the method we used to assess cardiac activity. To explain, the ambulatory assessment of cardiac activity might not be as accurate or as

sensitive to assess small changes compared to well-controlled laboratory monitoring. For instance, because less contextual information for data interpretation is available [230]. A third limitation is that we cannot rule out that explicit stress increased as a result of becoming aware of the stress and that this awareness for stress, in turn, masked potential reducing effects of the intervention. Future studies could address this by measuring stress continually.

In this study a low dropout rate was found. Low dropout rates are a strength in intervention studies and it could suggest that it is possible to implement an experimental intervention in daily life even when there is limited contact with researchers and none with a therapist. Nevertheless, the low adherence rates suggest that participants withdrew from the intervention without actually withdrawing from the study. Future studies need to carefully study how adherence to and effectiveness of the intervention can be optimized without resulting in higher dropout rates.

In summary, this is one of the first large-scaled RCTs looking at the effect of an EMI in sample with high stress levels. Findings suggest that the worry-reduction EMI with mindfulness exercises was not more effective in improving HRV or unconscious stress in individuals with high levels of work stress compared to individuals who repeatedly registered their emotions or a waitlist control group.

APPENDIX 1 Words used in the Implicit Association Test measuring implicit stress

Self category	Other category	Positive category	Negative category
ik (I)	zij (they)	boos (angry)	kalm (calm)
mij (me)	hen (their or theirs)	geïrriteerd (irritated)	evenwichtig (balanced)
mijn (mine)	hun (their or theirs)	gespannen (tense)	geduldig (patient)
mijzelf (myself)	het (it)	bang (afraid or scared)	vredig (peaceful)
zelf (self)	ander (other)	piekeren (worry)	rustig (calm or quiet)

APPENDIX 2 Means (SDs) of heart rate, work stress, worry, anxiety depression, mindfulness, and explicit affect at pre-, mid-, and post-intervention for each condition

	Experimental condition	Control condition	Waitlist condition
***n* at each time point**			
Pre-intervention[a]	44 | 41	44 | 39	40 | 38
Mid-intervention[a]	37 | 34	42 | 37	39 | 35
Post-intervention[a]	37 | 34	42 | 34	39 | 37
Outcome variables	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Heart rate			
Pre-intervention	73.84 (9.42)	69.45 (8.27)	70.59 (10.58)
Mid-intervention	71.33 (10.46)	73.40 (10.57)	66.71 (9.06)
Post-intervention	72.40 (10.21)	71.47 (11.81)	69.57 (9.77)
Work stress			
Pre-intervention	1.19 (0.26)	1.18 (0.15)	1.17 (0.15)
Mid-intervention	—	—	—
Post-intervention	1.16 (0.23)	1.18 (0.27)	1.16 (0.29)
Trait worry			
Pre-intervention	54.02 (9.05)	52.49 (11.00)	50.80 (10.75)
Mid-intervention	52.50 (9.86)	53.18 (10.92)	50.00 (11.27)
Post-intervention	49.68 (8.03)	51.00 (11.49)	48.44 (10.78)
State worry – frequency[b]			
Pre-intervention	4.16 (9.12)	3.44 (8.51)	3.20 (6.09)
Mid-intervention	4.61 (11.46)	2.98 (4.26)	4.41 (12.31)
Post-intervention	2.27 (5.19)	2.48 (6.20)	2.03 (3.17)
State worry – duration[c]			
Pre-intervention	20.57 (24.31)	22.63 (40.92)	12.25 (16.75)
Mid-intervention	21.72 (33.11)	26.51 (52.31)	18.22 (29.06)
Post-intervention	17.59 (37.15)	18.98 (41.54)	14.47 (26.11)
State worry – severity			
Pre-intervention	1.35 (0.51)	1.24 (0.45)	1.29 (0.67)
Mid-intervention	1.94 (0.72)	1.76 (0.91)	1.58 (0.82)
Post-intervention	1.88 (0.85)	1.52 (0.50)	1.61 (0.77)
Trait anxiety			
Pre-intervention	5.75 (3.03)	5.72 (3.09)	5.48 (3.43)
Mid-intervention	6.09 (3.48)	5.53 (3.26)	4.70 (3.32)
Post-intervention	5.16 (2.95)	6.08 (3.58)	5.33 (4.12)
Trait depression			
Pre-intervention	6.50 (2.95)	5.58 (3.28)	5.63 (3.85)
Mid-intervention	6.74 (3.31)	5.65 (3.40)	5.05 (3.54)
Post-intervention	5.51 (3.13)	5.79 (3.92)	5.14 (3.11)

	Experimental condition	Control condition	Waitlist condition
Mindfulness			
Pre-intervention	124.07 (14.73)	127.40 (17.17)	127.85 (14.23)
Mid-intervention	128.15 (15.93)	127.50 (17.53)	125.19 (13.86)
Post-intervention	129.84 (16.60)	130.61 (18.83)	126.83 (17.70)
Explicit negative affect			
Pre-intervention	24.91 (14.62)	26.16 (13.93)	23.55 (11.75)
Mid-intervention	25.89 (14.00)	22.85 (15.06)	24.21 (13.69)
Post-intervention	24.97 (14.99)	20.65 (12.85)	22.47 (15.54)
Explicit positive affect			
Pre-intervention	57.29 (16.20)	55.28 (15.75)	58.89 (13.52)
Mid-intervention	56.01 (18.21)	56.49 (19.67)	59.16 (16.27)
Post-intervention	57.20 (19.74)	57.68 (21.23)	62.02 (15.96)

[a]The first sample size reflects the number of participants that was available for analyses of the psychological outcomes and the second sample size reflects the number of participants that was available for the physiological data analysis.

[b]Indicated with the number of worry episodes per test day.

[c]Indicated with the number of minutes per test day.

APPENDIX 3 Results of primary and secondary outcome variables in the sample that was included in the intention-to-treat analysis

	Model 1		Model 2			
	Constant	Time[a]	Constant	Time[a]	Condition[b]	Time x Condition
Multilevel model						
RMSSD[c]	3.67 (0.05)	-0.02 (0.02)	3.73 (0.07)	-0.05 (0.04)	-0.06 (0.06)	0.03 (0.03)
24-hr data	[3.58, 3.77]	[-0.06, 0.03]	[3.59, 3.86]	[-0.12, 0.02]	[-0.17, 0.05]	[-0.02, 0.09]
Implicit negative affect	1.32 (0.06)	0.01 (0.03)	1.03 (0.10)	-0.03 (0.04)	0.27 (0.07)**	0.04 (0.03)
	[1.19, 1.44]	[-0.04, 0.06]	[0.85, 1.22]	[-0.11, 0.06]	[0.13, 0.42]	[-0.02, 0.10]
Implicit positive affect	1.78 (0.07)	0.02 (0.03)	1.53 (0.11)	0.01 (0.05)	0.25 (0.08)**	0.00 (0.04)
	[1.65, 1.92]	[-0.04, 0.08]	[1.32, 1.74]	[-0.08, 0.11]	[0.09, 0.41]	[-0.07, 0.08]
Implicit stress	-0.39 (0.03)	-0.04 (0.02)*	-0.37 (0.04)	-0.04 (0.03)	-0.02 (0.03)	0.00 (0.02)
	[-0.44, -0.33]	[-0.08, -0.01]	[-0.46, -0.28]	[-0.10, 0.01]	[-0.08, 0.05)	[-0.04, 0.04]
Heart rate[c]	65.56 (0.91)	0.09 (0.48)	63.96 (1.33)	0.63 (0.59)	1.85 (1.07)[t]	-0.63 (0.48)
24-hr data	[63.79, 67.34]	[-0.85, 1.02]	[61.35, 66.56]	[-0.53, 1.79]	[-0.27, 3.96]	[-1.56, 0.31]
Work stress[d]	0.15 (0.01)	-0.01 (0.01)	0.15 (0.02)	-0.01 (0.01)	0.00 (0.02)	0.01 (0.01)
	[0.13, 0.18]	[-0.02, 0.01]	[0.11, 0.19]	[-0.04, 0.02]	[-0.03, 0.03]	[-0.02, 0.03]
Trait worry	52.58 (0.91)	-1.36 (0.30)***	50.89 (1.47)	-1.18 (0.48)*	1.64 (1.12)	-0.18 (0.37)
	[50.79, 54.37]	[-1.95, -0.77]	[48.00, 53.78]	[-2.12, -0.24]	[-0.58, 3.85]	[-0.91, 0.55]
State worry severity	1.39 (0.06)	0.18 (0.05)**	1.33 (0.10)	0.14 (0.09)	0.06 (0.07)	0.05 (0.07)
	[1.28, 1.51]	[0.07, 0.28]	[1.14, 1.52]	[-0.03, 0.31]	[-0.08, 0.21]	[-0.09, 0.18]
Trait depression	5.94 (0.30)	-0.25 (0.15)[t]	5.39 (0.48)	-0.16 (0.24)	0.54 (0.37)	-0.08 (0.18)
	[5.35, 6.53]	[-0.54, 0.047]	[4.43, 6.34]	[-0.63, 0.31]	[-0.19, 1.27]	[-0.44, 0.28]
Trait anxiety	5.62 (0.27)	-0.09 (0.16)	5.31 (0.44)	-0.05 (0.26)	0.30 (0.34)	-0.04 (0.20)
	[5.08, 6.15]	[-0.42, 0.23]	[4.44, 6.18]	[-0.57, 0.47]	[-0.37, 0.96]	[-0.44, 0.36]
Mindfulness	126.08 (1.33)	1.47 (0.60)*	127.67 (2.15)	0.16 (0.95)	-1.55 (1.64)	1.30 (0.74)[t]
	[123.46, 128.69]	[0.28, 2.66]	[123.44, 131.91]	[-1.72, 2.04]	[-4.79, 1.70]	[-0.16, 2.76]
Explicit negative affect	24.84 (1.17)	-1.02 (0.64)	24.30 (1.89)	-1.18 (1.03)	0.53 (1.44)	0.17 (0.80)
	[22.54, 27.14]	[-2.28, 0.25]	[20.60, 28.00]	[-3.19, 0.84]	[-2.33, 3.39]	[-1.41, 1.74]

	Model 1		Model 2			
	Constant	Time[a]	Constant	Time[a]	Condition[b]	Time x Condition
Explicit positive affect	57.22 (1.32)	0.66 (0.73)	58.06 (2.13)	1.18 (1.17)	-0.83 (1.63)	-0.54 (0.92)
	[54.63, 59.81]	[-0.78, 2.09]	[53.88, 62.24]	[-1.11, 3.48]	[-4.05, 2.39]	[-2.33, 1.26]
GLMM						
State worry frequency	1.30 (0.11)	-0.08 (0.07)	1.28 (0.17)	-0.14 (0.11)	0.03 (0.13)	0.07 (0.08)
	[1.10, 1.51]	[-0.21, 0.06]	[0.94, 1.62]	[-0.35, 0.07]	[-0.23, 0.28]	[-0.10, 0.23]
State worry duration	3.16 (0.10)	0.08 (0.08)	3.00 (0.17)	0.10 (0.14)	0.16 (0.13)	-0.00 (0.11)
	[2.96, 3.37]	[-0.08, 0.25]	[2.67, 3.33]	[-0.17, 0.37]	[-0.09, 0.41]	[-0.21, 0.21]

Note. For every predictor the coefficient (standard error) and [95% confidence interval] is reported; GLMM = generalized linear mixed model; RMSSD = root mean square of successive differences.

[a]Time was coded as: 0 = first test day, 1 = second test day, 2 = third test day.

[b]Condition was coded as: 0 = waitlist condition, 1 = control condition, 2 = experimental condition.

[c]The models fitted for cardiac activity were all corrected for movement (acceleration in *g*).

[d]Work stress is operationalized as an imbalance between effort and reward.

***$p < .001$.

**$p < .01$.

* $p < .05$.

[t]$p < .10$.

Converging evidence that subliminal evaluative conditioning does not affect self-esteem or cardiovascular activity

06

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ABSTRACT

Background

Self-esteem moderates the relationship between stress and (cardiovascular) health, with low self-esteem potentially exacerbating the impact of stressors. Boosting self-esteem may therefore help to buffer against stress.

Objectives

Subliminal evaluative conditioning (SEC), which subliminally couples self-words with positive words, has previously been successfully used to boost self-esteem, but the existing studies are in need of replication. In this article, we aimed to replicate and extend previous SEC studies.

Methods

The first 2 experiments simultaneously examined whether SEC increased self-esteem (Experiment 1, n = 84) and reduced cardiovascular reactivity to a stressor in high worriers (Experiment 2, n = 77). On the basis of these results, the 3rd experiment was set up to examine whether an adjusted personalized SEC task increased self-esteem and reduced cardiac activity in high worriers (n = 81).

Results

Across the 3 experiments, no effects were found of SEC on implicit or explicit self-esteem or affect or on cardiovascular (re)activity compared to a control condition in which the self was coupled with neutral words.

Conclusions

The results do not support the use of the subliminal intervention in its current format. As stress is highly prevalent, future studies should focus on developing other cost-effective and evidence-based interventions.

INTRODUCTION

It is widely known that there is a negative relation between stress and health (e.g., [22]). This might be particularly relevant in people with low self-esteem as self-esteem is negatively associated with worrying [94], anxiety [231], and depression [231]. Moreover, a prospective study by Trzesniewski et al. [232] showed that low self-esteem in adolescence is a predictor for lower mental and physical health in adulthood even after controlling for relevant co-varying variables. Increasing self-esteem can therefore be important and might provide a buffer against stress. In the present study, we specifically focused on the effect of *implicit* self-esteem on psychological outcomes and physiological activity.

Implicit Self-Esteem

Current self-esteem interventions primarily target explicit processes, that is, explicit self-esteem that encompasses people's explicit beliefs or knowledge about themselves. Yet people may not always be aware of their self-esteem, and it is believed that attitudes towards oneself can affect behavior and stress responses at the implicit level [233]. According to different authors (e.g., [234, 235]), explicit and implicit processes originate from different information processing systems that operate simultaneously. From this perspective, explicit processes are based in the reflective system known for its rule-based processing that requires cognitive capacity. In this system, a response (e.g., a behavior) results from a conscious decision process. Implicit processes are based in the impulsive system, which consist of networks of associations. Perceptual input or processes in the reflective system can activate these associations, and the activation then spreads to related elements, concepts, or behaviors. In contrast to the reflective system, the impulsive system is fast and does not depend on cognitive effort. Moreover, the impulsive system is recognized to have a low threshold for incoming information [235]. Considering that self-esteem may also be represented as an implicit (or automatic or unconscious) concept, it might be appropriate to modify this implicit process.

Study Rationale

Stress research has only scarcely focused on the importance of implicit processes for health. Yet Brosschot, Verkuil, and Thayer [38] proposed that unreported processes (i.e., unconscious perseverative cognition or worry) play an important role in explaining prolonged physiological effects due to stress. That is, implicit mental representations of threats to oneself (such as implicit worries or implicit low self-esteem) are hypothesized to prolong the stress response beyond the presence of the actual stressor. These

prolonged physiological effects in turn lead to wear and tear effects on the body [28, 236].

A lot of research has been done on explicit worry and self-esteem, and its relation to increased physiological activation and its delayed recovery (e.g., [39, 237-239]). However, no research has looked whether implicit worry or self-esteem affects physiological activity. Therefore, the present study with three experiments focused on the effect of implicit self-esteem on physiological activity. Specifically, we aimed to experimentally *manipulate* implicit self-esteem as this allowed us to make statements about directionality and causality. Below we introduce the three experiments in which we aimed to increase implicit self-esteem, which represents the automatic or unconscious associations with the self-concept [80]. In Experiment 1, we attempted to replicate a previous study on subliminal evaluative conditioning (SEC) to increase implicit self-esteem [78]. In Experiments 2 and 3, we subsequently examined the effect of this self-esteem manipulation on physiological activity. This allowed us to examine if boosting implicit mental representations related to self-esteem indeed affect physiological activity, as hypothesized by Brosschot et al. [38].

Subliminal Evaluative Conditioning

SEC has been successfully used to increase implicit self-esteem [78]. Hereby, the self is repeatedly coupled with positive affective words and both stimuli are presented subliminally. With this, the self is assumed to acquire the value of the positive words. Using this procedure, Dijksterhuis [78] found higher implicit self-esteem in the experimental condition compared to the control condition (i.e., the self is coupled with neutral words). Grumm, Nestler, and Collani [79] reported similar effects in a larger sample, but no effect was found on explicit state self-esteem. A nearly identical SEC procedure was used by Jraidi and Frasson [240] and resulted in higher implicit self-esteem, learning performance, positive emotions, and delta-low-theta activity, which is indicative of higher concentration. Furthermore, Svaldi, Zimmermann, and Naumann [241] showed that SEC using slightly longer presentation times for stimuli and more trials resulted in higher implicit self-esteem. Using the same paradigm, Riketta and Dauenheimer [242] found higher levels of explicit self-esteem when self-referent words were coupled to positive words compared to negative words. Yet only explicit measures were studied, and these results might not directly translate to implicit outcomes. Importantly, these studies show that SEC has an effect size between medium and large. These initial findings seem promising, but the conclusions are limited due to issues of reliability concerning the assessment of implicit self-esteem. Specifically, previous studies measured implicit self-esteem with either (a) a shortened and unvalidated

version of the Implicit Association Test (IAT) [243] or with (b) the Initials Preference Task that has insufficient psychometric properties [220]. There is therefore need for studies that assess whether implicit self-esteem can indeed be enhanced using SEC. We set out to test this and additionally examined if enhancing implicit self-esteem reduces cardiovascular (re)activity.

Overview of Three Experiments

Our study's objective was to examine the effect of SEC on implicit self-esteem (Experiments 1 to 3) and physiological activity (Experiments 2 and 3). Overall, we hypothesized that when the self was subliminally coupled to positive words, this would increase implicit self-esteem and reduce cardiovascular (re)activity. The first two experiments were carried out simultaneously to study whether the original SEC was capable of increasing self-esteem (Experiment 1) and whether it was capable of dampening the negative physiological consequences of a stressor in at risk individuals, that is, high worrying participants (Experiment 2). On the basis of the results of Experiments 1 and 2, Experiment 3 was set up to study the effectiveness of an adjusted SEC task for increasing self-esteem and decreasing cardiovascular activity, again in high-worrying participants.

EXPERIMENT 1

We aimed to examine whether implicit self-esteem could be increased using SEC. Previous studies have found large effects using this procedure [78, 79], and we intended to replicate this effect using a more reliable assessment of implicit self-esteem. On the basis of previous research, it was hypothesized that individuals in the experimental condition (EC) would have higher self-esteem (both implicit and explicit) directly after coupling the self with the positive words compared to the control condition (CC). In order to gain insight into the duration of the potential effects of SEC, a follow-up measurement of implicit self-esteem and affect (2 hr after the SEC) was added to the protocol. Although long-term effects of SEC are unknown, other subliminal priming paradigms have shown that effects can be maintained after several minutes (i.e., between 15 and 43 min) and even 4 days [57, 244]. Therefore, it was hypothesized that implicit self-esteem and positive affect (both implicit and explicit) were higher, and negative affect (both implicit and explicit) were lower in the EC compared to the CC 2 hr after the manipulation. We checked for baseline differences of trait self-esteem, trait worry, and intermediately perceived stress and worry. Moreover, we explored whether the hypothesized effects were influenced (moderated) by trait self-esteem and worry.

Method

Participants. Participants were recruited at Leiden University, and the study was approved by the internal review board (nr. CEP 3033663498). No specific inclusion or exclusion criteria were used. To estimate the required sample size, the effect size of Dijksterhuis [78] and Grumm et al. [79] were averaged (resulting in a d = 1.15) and used in a power analysis [212]. Per condition, 11 participants were required to detect an effect with the alpha set at .05 (80% power). To detect smaller effects, we aimed to include 80 participants. Eighty-four participants completed the experiment; 76 females and 8 males with a mean age of 19.83 (SD = 2.26).

Materials.

Self-esteem manipulation. Subliminal evaluative condition, as used by Dijksterhuis [78], was used to manipulate implicit self-esteem. The sequence of the trials was as follows: (a) a row of 10 X's was shown for 500 ms, (b) *Ik* was displayed (Dutch for 'I') for 17 ms, (c) a positive word (in the EC) or a neutral word (in the CC) was displayed for 17 ms, and (d) this was followed by a random letter string. Participants decided whether the letter string started with a vowel or consonant. Fifteen different positive and neutral words were used (see Appendix 1). All words were presented twice, resulting in 30 trials, and five practice trials were used.

Implicit self-esteem. The IAT was used to measure implicit self-esteem [243]). The task was presented as a categorization task. In each trial, a word—that belonged to a specific category—was randomly presented in the middle of the screen. The different category names were displayed in the top-left and right of the screen. Participants were instructed to determine to which category the word belonged and to press the corresponding key as quickly as possible.

The task consisted of five blocks composed of either 20 or 60 trials. Blocks 3 and 5 are the critical blocks. In these blocks, two categories are presented on the left and two on the right side of the screen (see Appendix 1 for details). The task was administered twice using different words (see Appendix 1). The proposed scoring algorithm by Greenwald, Nosek, and Banaji [219] was used to calculate the IAT score.

Awareness check. An awareness check was included to determine whether participants consciously perceived the SEC stimuli. On the basis of the signal detection theory [245], a *d'* measure and its 95% confidence interval was calculated using the true hits and correct rejections of 42 discrimination trials. To obtain good accuracy scores, corrections were made of 1/(2 N) and 1-1/(2 N) with N = 42. If the confidence interval included zero, it was assumed that the participants did not consciously perceive the shown prime words. On the basis of this criterion, no participants were excluded from the analyses.

Questionnaires. Explicit state self-esteem was assessed using the 20-item State Self-Esteem Scale (SSES) [246]. Cronbach's alpha was considered high (.86). Affect was measured implicitly as well as explicitly. *Implicit affect* was measured using the Implicit Positive and Negative Affect Test (IPANAT) [191]. In this test, participants are shown nonsense words (e.g., VIKES) and they have to indicate to what extent those words express an emotion (e.g., sad). Five nonsense words were shown, and each word was coupled with 12 emotional adjectives (i.e., three adjectives per primary emotion [anxiety, anger, sadness, and happiness]). Resulting in 74 items and from this positive and negative implicit affect scores were calculated. As a measure of *explicit affect*, participants were asked to what extent they were currently experiencing the 12 emotional adjectives. Cronbach's alpha for positive and negative affect was adequate for both implicit and explicit affect (between .72 and .90). Trait self-esteem was assessed with the 10-item Rosenberg Self-Esteem Scale (RSES) [247]. The 16-item Penn State Worry Questionnaire (PSWQ) [94] was used to measure trait worry. Both instruments had high Cronbach's alpha (respectively .88 and .94).

Participants also indicated whether they had encountered any periods of stress or worry in the 2 hr between the first and second session. If so, participants registered the frequency and length of these periods of worry or stress. Plus the severity of these stressful events on a 5-point scale with 1 = 'not at all' and 5 = 'very much.'

Procedure. At the start of the experiment, all participants were consented. After answering demographic questions, participants were randomly allocated to the EC or CC. Participant and experimenter were blind to the allocated condition. Due to a programming error in the randomization scheme, more participants were allocated to the EC than to the CC (50/84, 60%). The SEC paradigm was followed by the IAT and SSES. A baseline measure of both the IAT and SSES was omitted, because it would risk giving away the true focus of the experiment (i.e., self-esteem). After completing the SSES, participants were informed that they could leave and were to return within 2 hr for the second part of the experiment. In part two of the experiment, participants answered questions concerning worry or stress episodes in the past 2 hr. Next, the second IAT, IPANAT, explicit affect measure, and the awareness check were completed. Participants were thanked and debriefed. Participants were told that we had aimed to increase (implicit) positive affect; however, participants were not yet told that the true aim was to increase (implicit) self-esteem. This knowledge could have influenced the trait self-esteem questionnaire that had to be filled in a week later. This questionnaire was completed a week after the experiment for two reasons. First, including the questionnaire at the start of the experiment could have given away the true aim of the experiment. Second, if the questionnaire was presented directly at the

end of the experiment, the self-esteem manipulation may have influenced the scoring and we believed it was unlikely that the potential effects of the SEC lasted for a week. Additionally, the PSWQ had to be filled in. After completing the two questionnaires online, participants were informed about the true aim of the experiment. Participants received money or course credit for participating.

Statistical analyses. Independent sample *t* tests were done to check whether the two conditions differed in trait self-esteem and worry (which were measured a week after completing the experiment). Furthermore, Bayes factors (of *t* tests) were estimated to determine whether the self-esteem manipulation differentially affected self-esteem and affect in the EC and CC (using Bayes factor package in R [version 0.99.484]). Bayes factors were used, because this type of hypothesis testing is more robust and is not biased in favor of rejecting the null-hypothesis compared to traditional hypothesis testing [248]. Given the expected direction for implicit and explicit self-esteem directly after the SEC paradigm, these analyses were tested one-sided. All other outcomes were tested two-sided. The classification system of Jeffreys [249] and Lee and Wagenmakers [250] was used to categorize the strength of the estimated Bayes factors.

Results

Descriptive statistics. For one participant, data of the second IAT and IPANAT were missing, and one participant failed to complete the trait worry and self-esteem questionnaire. Of the 84 participants, 34 were in the CC and 50 in the EC. The two conditions did not differ on descriptive variables including trait self-esteem and trait worry (see Table 1). Across the two conditions, the average trait self-esteem score was 10.05 (SD = 4.46) and the average trait worry was 51.17 (SD = 13.40). The number of stressful events and worry episodes that participants encountered between Parts 1 and 2 of the experiment did not differ between conditions. Across both conditions, 12 participants reported experiencing a stressful episode, with a mean frequency of 2.08 (SD = 1.50), a mean duration of 34.36 min (SD = 39.49), and a mean severity score of 1.45 (SD = 0.69). Thirty-seven participants reported experiencing at least one worry episode. The mean frequency of those episodes was 1.78 (SD = 0.98), and the mean duration in minutes was 18.62 (SD = 26.72).

TABLE 1 Baseline characteristics, biobehavioral, and outcomes variables per condition in Experiments 1 - 3

	Experiment 1		Experiment 2		Experiment 3	
	EC (n = 34)	CC (n = 50)	EC (n = 39 | 37)[a]	CC (n = 38 | 33)[a]	EC (n = 41 | 35 | 33)[b]	CC (n = 39 | 29 |32)[b]
Baseline variables						
Gender[c]	88%	94%	90%	82%	90%	85%
Age	19.82 (2.16)	19.85 (2.44)	20.41 (2.27)	20.16 (1.73)	20.32 (2.39)	20.49 (2.06)
Trait SE	9.49 (4.33)[d]	10.85 (4.59)[d]	9.90 (3.96)[d]	10.59 (4.17)[d]	12.10 (3.58)[d]	11.33 (4.96)[d]
Trait worry	50.53 (13.62) [d]	52.09 (13.23)[d]	55.05 (7.62)	54.97 (7.91)	53.54 (6.15)	55.21 (8.16)
SBP	—	—	119.18 (20.14)	120.66 (16.50)	121.92 (18.82)	127.81 (16.84)
DBP	—	—	59.91 (12.91)	61.02 (11.91)	69.58 (10.40)	71.45 (11.64)
HR[e]	—	—	78.49 (13.06)	76.85 (10.86)	76.43 (10.37)	78.72 (9.81)
RMSSD	—	—	—	—	37.05 (18.31)	36.16 (25.68)
Biobehavioral variables						
Coffee today	—	—	0.33 (0.66)	0.34 (0.67)	0.44 (0.78)	0.36 (0.81)
Cigarette today	—	—	1.33 (1.53)	1.17 (0.98)	0.15 (0.57)	0.00 (0.00)
Alcohol today[f]	—	—	0	0	0	0
Drugs today[f]	—	—	0	0	0	0
Medication use[f]	—	—	8	9	5	7
Current psychological treatment[f]	1	0	2	4	4	4
Outcome variables						
Implicit SE	0.55 (0.50)	0.36 (0.60)	0.62 (0.44)	0.51 (0.43)	0.69 (0.43)	0.69 (0.45)
Implicit SE, delayed effect	0.40 (0.48)	0.44 (0.42)	—	—	—	—
Explicit state SE	69.80 (4.89)	67.62 (5.86)	69.36 (10.56)	66.59 (10.82)	65.93 (9.04)	65.41 (11.18)
Implicit PA	3.02 (0.62)	2.99 (0.52)	2.92 (0.78)	2.97 (0.68)	3.21 (0.69)	3.09 (0.60)
Implicit NA	2.86 (0.53)	2.86 (0.53)	2.89 (0.67)	3.06 (0.43)	3.09 (0.44)	3.02 (0.48)

	Experiment 1		Experiment 2		Experiment 3	
	EC (n = 34)	CC (n = 50)	EC (n = 39 | 37)[a]	CC (n = 38 | 33)[a]	EC (n = 41 | 35 | 33)[b]	CC (n = 39 | 29 |32)[b]
Explicit PA	4.20 (0.79)	4.16 (0.90)	3.94 (0.85)	3.68 (0.89)	3.98 (0.88)	4.13 (0.82)
Explicit NA	1.67 (0.53)	1.72 (0.66)	1.89 (0.53)	2.12 (0.76)	1.74 (0.50)	1.70 (0.50)

Note. CC = control condition; DBP = diastolic blood pressure; EC = experimental condition; HR = heart rate; NA = negative affect; PA = positive affect; SBP = systolic blood pressure; SE = self-esteem; RMSSD = root mean square of successive differences.

[a] The first sample size reflects the number of participants included in the analyses of the psychological outcomes and the second sample size reflects the number of participants included in the physiological data analyses.

[b] The first sample size reflects the number of participants included in the analyses of the psychological outcomes, the second sample size reflects the number of participants included in the analyses of the blood pressure data and the third sample size reflects the number of participants in the analyses of the heart rate and heart rate variability data.

[c] Gender is represented by the percentage of women.

[d] It is considered a baseline variable, but the variable was actually measured a week after completing the experiment as inclusion of this measure at baseline would have risked giving away the true nature of the experiment.

[e] Heart rate is calculated from the blood pressure data in Experiment 2 and is measured using an electrocardiogram in Experiment 3.

[f] Indicated with the number of positive responses.

Direct effects. Contrary to the hypotheses, the estimated Bayes factor for implicit self-esteem indicated strong evidence that the data favored the null-hypothesis. Specifically, the data are 0.09 more likely under the alternative hypothesis than under the null-hypothesis ($t(82) = -1.63$). Moreover, the level of explicit state self-esteem did not differ between the two conditions. Again, the Bayes factor provided strong evidence for the null-hypothesis, with $t(82) = -1.85$, JZS $BF_{10} = 0.09$. In other words, SEC did not increase implicit or explicit self-esteem (see Table 1 for the means and SD's per condition). Exploratory analyses showed no moderation of the condition effect by trait worry or trait self-esteem.

Delayed effects. Bayes factor estimates for the second IAT found moderate evidence for the null-hypothesis, meaning that the conditions did not differ on implicit self-esteem 2 hr after the manipulation ($t(82) = 0.35$, JZS $BF_{10} = 0.24$). Furthermore, the estimated Bayes factors for both positive and negative implicit affect were in favor of the null-hypothesis (resp. $t(80) = -0.24$, JZS $BF_{10} = .24$ and $t(80) = -0.01$, JSZ $BF_{10} = 0.23$). Similar results were also found for explicit positive and negative affect (resp. $t(80) = -0.19$, JZS $BF_{10} = 0.24$ and $t(80) = 0.38$, JZS $BF_{10} = 0.25$). Summing up, there was no effect on implicit self-esteem and affect (both implicit and explicit) 2 hr after the SEC manipulation (see Table 1 for the means and SD's per condition).

EXPERIMENT 2

Previous research has shown that there is a negative association between self-esteem and cardiovascular functioning. Hughes [239], for instance, found higher systolic and diastolic blood pressure (resp. SBP and DBP) in reaction to negative feedback compared to positive feedback, and this effect was stronger for those with low compared to high self-esteem. Furthermore, Elfering and Grebner [251] showed that—in response to public speaking challenges—the habituation in blood pressure was faster in individuals with higher trait self-esteem. Moreover, Greenberg et al. [238] found that individuals with higher self-esteem had lower physiological arousal (i.e., skin conductance) in response to stress. Notable is the finding by Rector and Roger [252] that individuals who received a manipulation to increase state self-esteem had a lower heart rate (HR) in response to a stressful social performance task compared to those who received a neutral manipulation. In line with these laboratory studies, Smith, Birmingham, and Uchino [253] found a positive association between ambulatory measured social evaluative threat and blood pressure. In a related study, Levy et al. [57] subliminally primed older individuals with words related to either positive or negative age stereotypes (e.g., wise, insightful or Alzheimer and decline) and cardiovascular

activity was continuously measured during a stressful task. Results showed that positive priming directly decreased blood pressure and skin conductance and attenuated the responses during the stressful task. That is, it appeared to protect against stress-related physiological reactivity whilst negative priming had the opposite effect. These studies suggest that high self-esteem may act as a buffer against the negative physiological effects of a stressor. Considering this, it will be interesting to see if increasing implicit self-esteem using SEC can provide a buffer against stress and results in a reduced cardiovascular reaction to a stressor.

To date, no study has investigated whether SEC can provide a buffer against physiological stress. The aim of this experiment—which was conducted simultaneously with Experiment 1—was to examine whether SEC had an effect on self-esteem and cardiovascular (re)activity to a stressor. On the basis of previous literature, an increase in implicit and explicit self-esteem was expected in the EC compared to the CC. With regard to the cardiovascular activity, we expected (a) a decrease in blood pressure and HR during the SEC compared to baseline (as a direct effect) and (b) a decrease in blood pressure and HR reactivity in response to a stressor in the EC compared to the CC.

Method

Participants. The study was approved by the internal review board of Leiden University (CEP nr. 8812891384) and students were included if they (a) had not participated in Experiment 1 and (b) had a minimum score of 45 or higher on the PSWQ. This cut-off score can be used to screen for generalized anxiety disorder [104] and ensured that participants were high worriers (and thus at a greater risk for CVD and low self-esteem, making it a clinically interesting sample). Participants were selected based on their level of worry and not self-esteem, because we did not want to give away the focus of the study by using a self-esteem questionnaire. Sample size was based on the power analysis reported in Experiment 1. Seventy-seven individuals participated, including 11 males. The mean age was 20.29 (SD = 2.01).

Materials. The SEC paradigm and questionnaires were identical to Experiment 1. In contrast to Experiment 1, all measures were completed directly after the SEC paradigm and no follow-up measures were conducted. Blood pressure was measured continuously throughout the experiment using the Finometer MIDI (Finapres Medical Systems BV, the Netherlands) by placing a cuff around the middle finger of the nondominant hand. SBP and DBP were computed using a customized script in Matlab (version R2012b). Pulse in beats per minute was calculated from the blood pressure data, because it can be used as an indicator of HR. To obtain a baseline measure of

physiological activity, a 10-min nature documentary was shown. The first 9 min were used to recover from previous activity, and the final minute was used to calculate a baseline measure of SBP, DBP, and HR.

Procedure. People who were interested in participating could complete the PSWQ online to determine whether their worry level was sufficiently high (i.e., 45 or higher). If this was the case, a laboratory appointment was scheduled. During the laboratory appointment, participants were consented, and they were connected to the apparatus used to measure physiological activity during the entire experiment. Next, participants answered demographic and biobehavioral questions after which the 10-min nature documentary was shown. The SEC paradigm automatically started at the end of the movie, and participants were randomized into either the EC or CC. Afterwards, the experimenter entered the room and started the stress induction, which was a speech preparation based on Field and Powell [254]. Participants were told that they had to give a speech at the end of the experiment that reflected their opinion on the unrest in Syria (which was an important and recurring news item at the time of the experiment). Participants were told that the speech had to be given in front of a camera, and that they would be judged by the experimenter on their social and communication skills. Other psychologists from the department would also view the recording at a later moment and perform similar ratings. At this point, the experimenter setup a camera next to the computer and indicated that the camera would start recording at the start of the speech. Two anticipation periods were included; these periods could be used for preparation and making notes. The first one lasted 2 min and was scheduled directly after the stress induction instructions. This was followed by the IAT, IPANAT, explicit affect measure, awareness check, and the second anticipation period (lasting 1 min). After this, participants were informed that no speech had to be given and, similar to Experiment 1, they received the first debriefing. A week later, participants completed the RSES online, and they received the second (true) debriefing. Participants were rewarded money or course credit.

Statistical analyses. The analyses of the psychological outcome measures were similar to Experiment 1; however, all analyses were tested two-sided (because the effect of SEC on stress induction had not been previously studied). For the physiological outcomes—SBP, DBP, and HR—mean levels per minute were calculated for the manipulation, the anticipation 1 and 2 phases. To ensure the reliability of the physiological data, averages were only analyzed when less than 35% of the data in that minute was used to calibrate the blood pressure signal by the Finometer.

Multilevel analyses were used to examine whether there was a direct effect of SEC on cardiac activity (i.e., SBP, DBP, and HR). For each of the physiological

outcomes, a multilevel model was built including the predictor time (i.e., 0 = last minute of baseline, 1 to 3 = 3 min of the manipulation phase), condition (i.e., 0 = CC, 1 = EC) and Time X Condition. The interaction allowed us to examine whether cardiac activity during the manipulation decreased as a result of SEC. Furthermore, to examine whether SEC affected cardiac reactivity to stressors, three additional models were built with similar predictors. However now, the predictor time included not only the baseline and the manipulation phase (3 min) but also the first anticipatory stressor phase (2 min) and the second anticipatory stressor phase (1 min).

Besides focusing on the hypothesis that the self-esteem manipulation would affect cardiovascular reactivity, we explored whether trait self-esteem was associated with cardiovascular reactivity to the stressor. Enhanced reactivity to the stressor might be expected in people with low self-esteem, if self-esteem is indeed related to somatic health. To do so, multilevel analyses were used with cardiovascular responses to the speech preparation as outcome (i.e., anticipatory stressor phases) and trait self-esteem as predictor. The models were controlled for baseline levels of physiological activity.

Results

Descriptive statistics. Of the 77 participants, 38 were in the CC and 39 were in the EC. The conditions did not differ on the descriptive or biobehavioral variables, vor on trait worry or trait self-esteem (see Table 1).

One participant stopped with the experiment after the IAT. For this participant, only part of the data were available and no physiological data were saved. Physiological data of seven participants were not included (although their exclusion did not change the results). Therefore, the physiological data of 70 participants were analyzed. The baseline levels of SBP, DBP, and HR did not significantly differ between conditions (Table 1).

Psychological outcomes. The estimated Bayes factor for implicit self-esteem indicated anecdotal evidence—formerly known as 'barely worth mentioning'—for the null-hypothesis, with $t(75) = -1.06$ and JZS $BF_{10} = 0.38$. The same was true for explicit self-esteem, with $t(74) = -1.13$ and JZS $BF_{10} = 0.41$. Moreover, exploratory analyses indicated that there was no moderation of condition by trait worry or trait self-esteem. Furthermore, moderate to anecdotal evidence for the null-hypothesis was found for implicit positive and negative affect, and explicit positive and negative affect (implicit positive affect: $t(74) = 0.33$, JZS $BF_{10} = 0.25$; implicit negative affect: $t(74) = 1.26$, JSZ $BF_{10} = 0.47$; explicit positive affect: $t(74) = -1.33$, JZS $BF_{10} = 0.51$ and explicit negative affect: $t(74) = 1.54$, JZS $BF_{10} = 0.66$). All in all, implicit and explicit self-esteem and affect did not differ between conditions as a result of SEC (see Table 1 for means and

SD's per condition).

Physiological outcomes. To examine whether SEC directly affected cardiac activity during the manipulation phase, multilevel models were built for SBP, DBP, and HR (see Table 2). The nonsignificant interaction effects show that SBP, DBP, and HR did not differ significantly over time between conditions (resp. B = −0.46 with p = .818, B = −0.12 with p = .923 and B = −0.02 with p = .990). This indicates that SEC did not affect cardiac activity during the manipulation phase.

The multilevel models for SBP, DBP, and HR showed an increase in physiological activity over time for all participants, resp. B = 4.14 with p < .001, B = 2.13 with p < .001, and B = 1.84 with p < .001 (see Table 2). Specifically, physiological activity increased at the start of the stressor (anticipatory stressor phase 1) and remained high during the second anticipatory stressor phase (see Figure 1). However, contrary to our hypothesis, the Time x Condition interaction was not significant for any of the physiological outcomes. This indicates that participants in the EC did not have a lower cardiovascular response in reaction to the stressor compared to the CC.

Moreover, the multilevel models showed that trait self-esteem was negatively associated with increased SBP and DBP in response to the stressor (resp. B = −0.89, p < .001 and B = −0.31, p = .003). Trait self-esteem was not significantly associated with the HR response to the stressor (B = −0.25, p = .074). Considering that SEC was not effective, we also explored whether cardiovascular reactivity in response to the stressor varied as a function of state self-esteem and implicit self-esteem. However, cardiovascular reactivity to the stressor was not associated with state self-esteem (SBP: B = 0.06, p = .462; DBP: B = 0.04, p = .318; HR: B = 0.06, p = .276) or implicit self-esteem (SBP: B = 0.30, p = .877; DBP: B = 1.54, p = .115; HR: B = 1.35, p = .301).

TABLE 2 Results of the multilevel models predicting cardiac activity in Experiments 2 and 3

	Systolic blood pressure			Diastolic blood pressure			Heart rate[a]			Log-transformed RMSSD		
Predictor	B (SE)	*t*	*p*	B (SE)	*t*	*p*	B (SE)	*t*	*p*	B (SE)	*t*	*p*
Experiment 2												
Effect of SEC during manipulation phase												
Intercept	123.12 (2.70)	45.55		61.49 (1.74)	35.39		77.81 (1.88)	41.30				
Time	2.53 (1.46)	1.73	.084	1.30 (0.94)	1.39	.166	-0.11 (1.02)	-0.11	.915			
Condition	-2.50 (3.71)	-0.67	.501	-1.56 (2.38)	-0.65	.514	1.85 (2.58)	0.72	.474			
Time X Condition	-0.46 (1.99)	-0.23	.818	-0.12 (1.28)	-0.10	.923	-0.02 (1.39)	-0.01	.990			
Effect of SEC during manipulation phase and anticipatory stressor phases												
Intercept	121.98 (2.23)	54.60		60.87 (1.35)	45.15		75.60 (1.57)	48.01				
Time	4.14 (0.62)	6.70	.000**	2.13 (0.37)	5.72	.000**	1.84 (0.43)	4.23	.000**			
Condition	-2.90 (3.07)	-0.94	.345	-1.99 (1.85)	-1.08	.282	2.29 (2.16)	1.06	.290			
Time X Condition	-0.16 (0.85)	-0.19	.852	0.24 (0.51)	0.46	.644	-0.33 (0.60)	-0.55	.584			
Experiment 3												
Intercept	130.56 (2.84)	45.92		72.57 (1.74)	41.80		80.62 (1.61)	50.10		1.46 (0.03)	45.53	
Time	3.73 (1.52)	2.45	.015*	1.42 (0.93)	1.53	.128	0.07 (0.86)	0.08	.938	0.03 (0.02)	2.00	.047*
Condition	-6.51 (3.84)	-1.69	.092	-2.19 (2.35)	-0.93	.352	-2.90 (2.26)	-1.28	.201	0.04 (0.04)	0.88	.378
Time X Condition	-1.65 (2.05)	-0.80	.424	-0.46 (1.25)	-0.37	.712	0.09 (1.21)	0.07	.943	-0.03 (0.02)	-1.09	.277

Note. B = coefficient; RMSSD = root mean square of successive differences; SE = standard error of the coefficient.

[a] In Experiment 2 heart rate is calculated from the blood pressure data and in Experiment 3 heart rate is measured using an electrocardiogram.

* = $p < .05$.

** = $p < .01$.

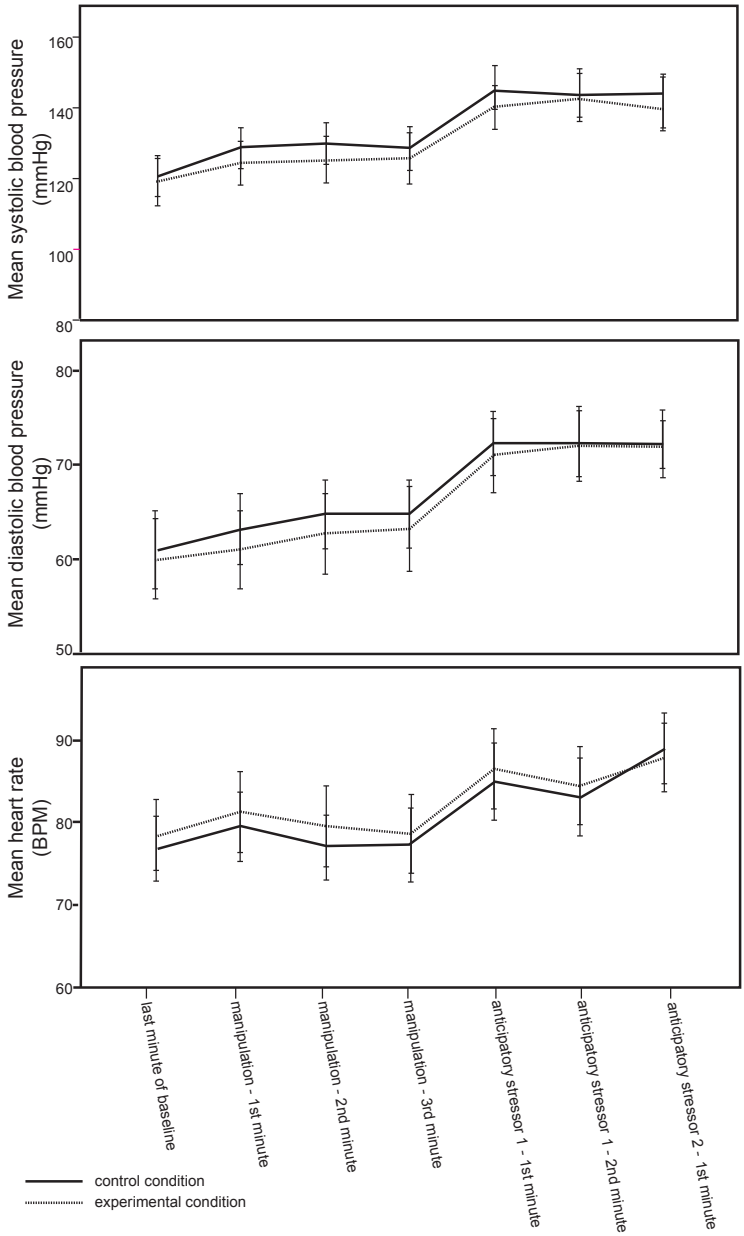

Figure 1 Line graphs representing the mean systolic and diastolic blood pressure, and heart rate in beats per minute (BPM) per condition during baseline, the self-esteem manipulation, and during the anticipatory stressor periods (Experiment 2). Error bars represent ± 2 SE.

EXPERIMENT 3

The findings of Experiment 1 and 2 suggest that SEC, in its current format, is ineffective in increasing self-esteem, decreasing cardiovascular activity and cardiovascular reactivity in response to a stressor. Therefore, the aim of the third experiment was to use an adjusted, 'personalized' and therefore more 'intense' version of SEC. In addition, a personalized and therefore more 'sensitive' version of the IAT was used. Together they were expected to result in a larger effect. The performed adjustments were based on changes that have been made to the original IAT by Olson and Fazio [255]. Specifically, Olson and Fazio personalized the IAT by replacing the more general category labels *pleasant* and *good* with respectively *I like* and *I don't like*. The personalized IAT thereby focuses more on personal attitudes versus generally held attitudes. Multiple experiments have indeed shown that this personalization reduced the extrapersonal associations. That is, associations that are available in memory but are irrelevant to one's own evaluation (e.g., other people's attitude about what is considered pleasant) [255-257]. Additionally, the personalized IAT had a stronger relation to behavioral intentions and behavior, and was better able to detect attitude change compared to the original IAT. In a like manner, we personalized the SEC labels (i.e., change 'I' to 'I am'), which was expected to result in a larger positive effect on self-esteem. To explain, in a personalized SEC task the positive words directly target the person (i.e., 'I am') instead of targeting the *self* (i.e., 'I'), which might represent a more generally held view of the self, for example, how one *should see* oneself.

It was investigated whether the personalized SEC increased implicit self-esteem, as measured by the personalized self-esteem IAT, and directly decreased cardiovascular activity. In order to study the effect on cardiovascular activity more accurately, the cardiovascular reactivity to a stressor was not included in the current experiment, because the inclusion of a stressor might mask potential (small) effects of SEC on cardiovascular activity. Considering that—as mentioned above—a subliminal positive priming paradigm has been shown to directly reduce blood pressure [57], we expected a decrease in cardiovascular activity as a direct result of SEC. Additionally, the effect of personalized SEC on explicit self-esteem and affect (both implicit and explicit) were explored during the experiment.

Method

Participants. The study was approved by the internal review board of Leiden University (CEP nr. 2989963000). High-worrying participants were selected using the same procedure and inclusion criteria as Experiment 2. However, participants were

only included when they had not participated in either Experiment 1 or 2. A power analysis, using the averaged effect size of Dijksterhuis [78], Grumm et al. [79], and Experiment 1 and 2 (i.e., d = 0.73), indicated that 25 participants per condition was sufficient to find an effect (with α = .05 and 80% power). To allow for potential exclusion, a higher number (i.e., n = 81) of participants were included (88% female) with a mean age of 20.40 (SD = 2.22).

Materials. The materials were largely equivalent to Experiment 2; only the self-esteem manipulation (SEC) and measure of implicit self-esteem (IAT) were adjusted. The SEC was personalized by the following change: instead of displaying *Ik* (Dutch for 'I'), the words *Ik ben* (Dutch for 'I am') were shown. Furthermore, the personalized version of the self-esteem IAT was used [258]. This IAT has the same arrangement of blocks, but the positive and negative category labels were replaced by *I like* and *I don't like* (in Dutch respectively 'ik vind dit leuk' and 'ik vind dit niet leuk'). In line with Experiment 1 and 2, five words were used per category. This is in contrast with Olson et al. [258] who used 10 or 20 different words per category. However, Greenwald, McGhee, and Schwartz [217] found comparable effects for IAT's that used either five or 25 words per category. Lastly, error feedback was removed [255, 258].

SBP and DBP were measured using the same equipment as in Experiment 2. HR and heart rate variability (HRV) were measured by placing three electrodes on the upper body using the BIOPAC MP150 system [BIOPAC Systems Inc., USA]. HRV refers to the variability and periodic changes in HR (i.e., variation in inter-beat intervals) and is a measure of parasympathetic nervous system activity [35, 259]. The root mean square of successive differences (RMSSD) was used as an index of HRV. A customized script in Matlab (version R2012b) was used to compute SBP, DBP, HR, and RMSSD. The data was visually inspected to detect and exclude incorrectly identified R-peaks. Similar to Experiment 2, the final minute of the documentary was used as a baseline measure of cardiac activity.

Procedure. The procedure was similar to Experiment 2, except that this time only cardiac activity was measured and no reactivity to a stressor. The experiment began by signing the informed consent. Afterwards participants were connected to the apparatuses that measured cardiac activity throughout the experiment. The sequence of tasks was comparable to Experiment 2, but without the stress induction. After completing all the tasks, participants received a first debriefing (like Experiment 1 and 2). A week later, participants completed the RSES online and a second (true) debriefing was given. Participants received money or course credit for participating.

Statistical analyses. The psychological outcome measures were analyzed in the same way as in Experiment 2. For SBP, DBP, HR, and RMSSD mean scores

were calculated for the manipulation phase. Again, the blood pressure data was only analyzed when less than 35% of the data in a minute was used to calibrate the blood pressure signal.

To examine whether SEC had a direct effect on cardiac activity in the absence of a stressor, multilevel models were built for each dependent variables (i.e., SBP, DBP, HR, and RMSSD). The models included the predictor time (i.e., 0 = final minute of baseline, 1 to 3 = 3 min of the manipulation phase), condition (i.e., 0 = CC, 1 = EC) and the interaction between time and condition. This enabled us to examine whether cardiac activity changed over time as a result of SEC and whether this change was different between conditions.

The RMSSD data was log-transformed. The untransformed means and standard deviations are reported in the Results. An additional Pearson correlation was done to explore whether HR calculated using the blood pressure data (as was done in Experiment 2) was positively associated with HR as measured with the electrocardiogram (i.e., considered the more standard measurement).

Results

Descriptive analyses. One participant stopped with the experiment while watching the documentary. Resulting in 80 participants, of whom 39 were allocated to the CC and 41 to the EC. The descriptive variables, biobehavioral variables, trait worry, and trait self-esteem did not differ between conditions (see Table 1).

Physiological data of 13 participants was excluded from the analyses (i.e., inclusion of these participants did not change the overall found results). Moreover, blood pressure data of three participants was excluded, and HR and RMSSD data of two participants was excluded. So the blood pressure analyses included data of 64 participants and the HR/RMSSD analyses included data of 65 participants. The baseline levels of SBP, DBP, HR, and log-transformed RMSSD did not significantly differ between conditions (see Table 1). In the final sample, there was a significant positive correlation between HR calculated using the blood pressure data and HR measured with an electrocardiogram (r = .99, p < .001).

Psychological outcomes. For implicit and explicit self-esteem, the estimated Bayes factors found moderate support for the null-hypothesis (resp. $t(78) = -0.08$, JSZ $BF_{10} = 0.23$ and $t(78) = -0.23$, JSZ $BF_{10} = 0.24$). Exploratory analyses again showed that there was no moderation of condition by trait worry or trait self-esteem. The results for implicit positive and negative affect and explicit positive and negative affect were comparable to the self-esteem results (implicit positive affect: $t(78) = -0.80$, JSZ $BF_{10} = 0.31$; implicit negative affect: $t(78) = -0.73$, JSZ $BF_{10} = 0.29$; explicit positive affect:

$t(78) = 0.76$, JSZ $BF_{10} = 0.30$ and explicit negative affect: $t(78) = -0.43$, JSZ $BF_{10} = 0.25$). In short, the levels of self-esteem and affect did not differ between the two conditions. The means and standard deviations per condition are displayed in Table 1.

Physiological outcomes. As can be seen in Table 2, the interaction between time and condition was not significant for SBP, DBP, HR, or RMSSD. This demonstrates that the change over time in cardiac activity during the manipulation phase did not differ significantly between the EC and CC. So, SEC did not have an impact on cardiac activity. Yet there was a significant effect of time on SBP and RMSSD. As can be seen in Figure 2 and Table 2, SBP and RMSSD increased slightly for all participants over time (resp. B = 3.73, $p = .015$ and B = 0.03, $p = .047$).

GENERAL DISCUSSION

In three experiments, we examined whether SEC increased implicit and explicit self-esteem by repeatedly coupling the self with positive affective words (subliminally), thereby testing whether increased self-esteem moderates the effect of a stressor. Altogether, the experiments failed to proof the effectiveness of SEC for improving self-esteem, affect, cardiovascular activity, and reactivity. As implicit self-esteem was not increased using SEC, we were unable to examine whether an implicit process manipulation can affect physiology activity. In other words, the findings failed to test whether unconscious or unreported processes can have an effect on physiological activity [38]. The results from Experiment 2 showed that individuals with high trait self-esteem had lower SBP and DBP responses to the stressor. Specifically, all individuals showed an increased cardiovascular response in reaction to the stressor, but this increase in reactivity was higher in individuals with low trait self-esteem and greater reactivity in response to a stressor is associated with poorer cardiovascular health [260]. However, this finding did not vary as a function of state self-esteem or implicit self-esteem. This latter finding is not in line with the idea that unconscious levels of stress can be associated with physiological activity [38], but the finding must be interpreted with caution as it is based on exploratory analyses.

In Experiment 1, it was found that SEC did not increase implicit or explicit self-esteem directly after the manipulation. Likewise, 2 hr after the manipulation, no effects were found on implicit self-esteem or on affect (both implicit and explicit). In Experiment 2, similar null-findings were obtained for self-esteem and affect (both implicit and explicit) in high worrying participants. Additionally, SEC had no effect on cardiovascular reactivity (i.e., SBP, DBP, and HR) in response to a stressor. In Experiment 3, the effect of a personalized SEC task was examined in high worrying participants and implicit

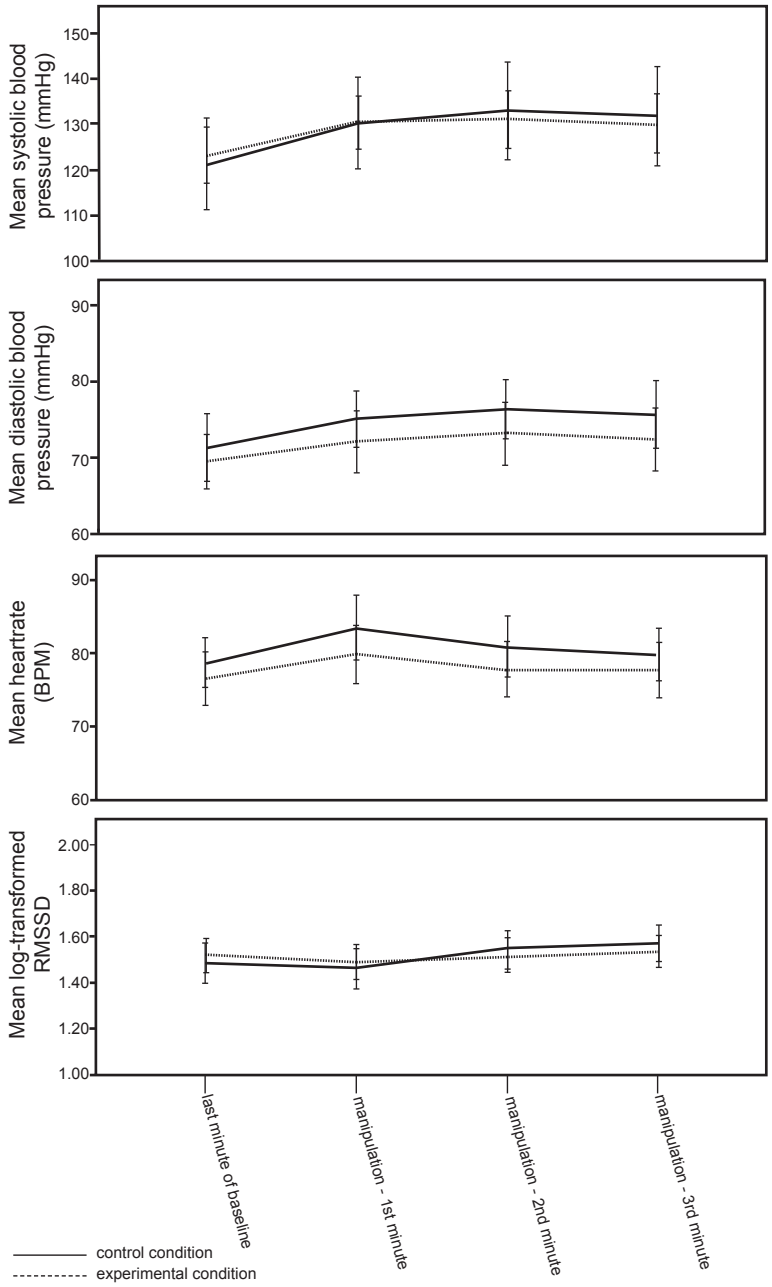

Figure 2 Line graphs representing the mean systolic and diastolic blood pressure, heart rate in beats per minute (BPM), and the root mean square of successive differences (RMSSD) per condition during baseline and during the self-esteem manipulation (Experiment 3). Error bars represent ± 2 SE.

self-esteem was measured in a personalized manner. Again, SEC had no effect on self-esteem, affect or on cardiac activity during the experiment. However, an increase over time in SBP and RMSSD was observed in all participants.

Explaining Null-Findings

Our findings are in contrast with previous research on SEC (e.g., [78, 79]). One strength of the current studies—when compared to these previous studies—are the consistent findings across three studies with large sample sizes (*n* between 77 and 84). Several explanations can be brought forward to explain the difference in findings. First, in the current studies, a different version of the IAT was used to measure implicit self-esteem. Specifically, a validated measure of the IAT [243] was used instead of a shortened version of the IAT, which was used in the previous studies (i.e., [78, 79]). By using fewer trials in a reaction time task—like the IAT—the measure is more vulnerable to problems of unreliability [220]. Therefore, it is possible that previously reported positive effects on implicit self-esteem are the result of an inaccurate measurement of implicit self-esteem.

Although the original IAT is less vulnerable to unreliability than the shortened version, the IAT itself might reduce the effects of SEC. To explain, the IAT pairs self-words with either positive or negative words and in this way could be considered a manipulation of implicit self-evaluations. However, if there was an effect of SEC, it seems unlikely that this effect was completely mitigated with the use of the original IAT as 50% of trials were positive and 50% were negative, and previous evaluative conditioning studies have found effects on this measure (e.g., [261]).

Another explanation for the null-indings relates to the sample of high worrying participants that were targeted in Experiments 2 and 3. As there is a negative association between worry and self-esteem [94], it is conceivable that the negative self-image in high-worrying individuals is more heavily ingrained compared to low-worrying individuals. Therefore, it might be more difficult to change implicit self-esteem in high-worrying individuals using SEC. Yet the effect of SEC on self-esteem was not moderated by trait worry or trait self-esteem in Experiments 1 to 3. This indicates that initial levels of worry (or self-esteem) did not have an impact on the effectiveness of SEC.

Changing Implicit Attitudes

The null-findings regarding SEC are inconsistent with the dual-system theory [234, 235], because an associative learning procedure that targeted self-related associations did not affect implicit self-esteem. Even though research has shown that implicit attitudes can change [262, 263], the specific process and the number of required trials

underlying this attitude change are not fully known. Gregg et al. [262] examined the process of attitude change by using a series of experiments in which the induction and reversing of implicit attitudes for fictional social groups was studied. The results demonstrated that implicit attitudes—once formed—are quite resistant to change. Nevertheless, Rydell et al. [263] showed that change in implicit attitudes can be accomplished (albeit more slowly), but that change happens linearly. That is, when providing more counter attitudinal information (e.g., 'I' + 'smart' in individuals with low self-esteem), more change in implicit self-esteem is obtained. These studies, however, used supraliminal information to change implicit attitudes, and it is unknown whether this change can also be expected with subliminally presented stimuli. A meta-analysis suggests that the effectiveness of evaluative conditioning varies depending on whether the conditioned or unconditioned stimuli is presented subliminally or supraliminally [264]. To date, a comprehensive study incorporating a cross-over design in which the conditioned and unconditioned stimuli are presented subliminally and supraliminally is missing. Additionally, it is unknown how many trials would be needed to accomplish a change in implicit attitudes, making this an interesting venue for future research.

Limitations

A limitation is that no baseline measure of state self-esteem was included. It is therefore possible that there were baseline differences between conditions, and these differences could have obscured an increase in self-esteem in the EC. Yet it is unlikely that baseline differences in implicit self-esteem have masked the effect of SEC. First, even though the chance exists that there were baseline differences in self-esteem between conditions in one experiment, the chances are low that this would have occurred in all three experiments, especially considering the large sample sizes. Second, trait self-esteem did not differ between conditions. Altogether, it is improbable that baseline differences in self-esteem are the reason for the null-findings.

A second limitation pertains to the measurement of implicit self-esteem. Psychometric properties of implicit measures are generally considered to be weak [220] and may not correctly measure implicit attitudes. Nevertheless, the IAT is considered the most promising (e.g., acceptable stability over time and predictive validity) [220, 221].

Another limitation is the unequal distribution of males and females across the three experiments (88% female, 213/242). It would be useful to examine whether the findings generalize to male populations.

Conclusion

No effects were found of SEC on implicit or explicit self-esteem or affect in either the general student population or in high-worrying students. Furthermore, SEC had no effect on cardiac reactivity to a stressor or on cardiac activity in high-worrying students. It was shown that individuals with higher trait self-esteem had lower SBP and DBP in response to the stressor, possibly suggesting that people high in self-esteem show lower cardiovascular responses to stressful events. Our results do not support the use of SEC as an intervention. Future studies should more thoroughly examine whether subliminal stimuli—compared to supraliminal stimuli—can indeed be used to change implicit attitudes, and whether increasing the number of SEC trials has an effect on the outcomes. As stress is common and is associated with a range of negative consequences, it is important that—preferably short and cost-effective—evidence-based interventions become available.

APPENDIX 1 Methodological details of the subliminal evaluative conditioning task and the Implicit Association Test

Words used in the subliminal evaluative conditioning task (Experiments 1-3)

Experimental condition	Control condition
warm (warm)	balpen (ball pen)
lief (sweet)	emmer (bucket)
aardig (nice)	duim (thumb)
oprecht (sincere)	ingang (entrance)
eerlijk (honest)	deur (door)
mooi (beautiful)	voetpad (footpath)
vrolijk (cheerful)	hek (fence)
slim (smart)	raam (window)
sterk (strong)	lade (drawer)
wijs (wise)	staan (to stand)
gezond (healthy)	melk (milk)
leuk (funny)	jas (coat)
blij (happy)	tas (bag)
prettig (nice)	bord (board)
positief (positive)	scherm (screen)

Note. The positive words in the experimental condition are derived from Dijksterhuis (2004) and the neutral words in the control condition are derived from De Houwer, Hendrickx, and Baeyens (1997).

Words used in the Implicit Association Test (Experiment 1[a] - Experiment 2)

Self category	Other category	Positive category	Negative category
ik (I)	zij (they)	geluk (happiness)	bom (bomb)
mezelf (myself)	anderen (others)	zomer (summer)	kanker (cancer)
mij (me)	hun (their or theirs)	lach (smile)	coma (coma)
zelf (self)	zjin (his)	strand (beach)	gemeen (mean)
mijn (mine)	haar (her)	zon (sun)	hel (hell)

Note. Words were selected from Dijksterhuis (2004).
[a]These words were only used in the first Implicit Association Test.

Words used in the Implicit Association Test (Experiment 1[a])

Self category	Other category	Positive category	Negative category
ik (I)	zij (they)	vreugde (joy)	dood (death)
mezelf (myself)	anderen (others)	warmte (warmth)	gif (poison)
mij (me)	hun (their or theirs)	plezier (pleasure)	pijn (pain)
zelf (self)	zjin (his)	paradijs (paradise)	tragedie (tragedy)
mijn (mine)	haar (her)	vrede (peace)	ziekte (sickness)

Note. Words were selected from Greenwald and Farnham (2000).
[a]These words were only used in the second Implicit Association Test.

Words used in the Implicit Association Test (Experiment 3)

Self category	Other category	Positive category	Negative category
ik (I)	zij (they)	vrijheid (freedom)	moord (murder)
mezelf (myself)	anderen (others)	liefde (love)	ziekte (sickness)
mij (me)	hun (their or theirs)	vrede (peace)	ongeluk (accident)
zelf (self)	zjin (his)	vriend (friend)	dood (death)
mijn (mine)	haar (her)	plezier (pleasure)	vergif (poison)

Note. Words were selected from Olson and Fazio (2004).

Category names and the number of traisl per block as used in the Implicit Association Test

Block	Left categor(y)(ies)	Right category (y)(ies)	Number of trials
1.	self	other	20
2.	positive	negative	20
3.	self	other	20 practice trials + 40
	positive	negative	
4.	negative	positive	20
5.	self	other	20 practice trials + 40
	negative	positive	

Note. Words were selected from Olson and Fazio (2004).

General discussion

07

INTRODUCTION

Human beings are prone to experience stress [5, 6] and this is of interest because research has repeatedly shown that experiencing stress has a negative effect on health [11-17], including cardiovascular health [18-24]. The negative health effect is recognized to occur as a result of prolonged physiological stress responses (like prolonged decreases in heart rate variability [HRV]) [10, 12, 25]. Most research to date has focused on increased physiological responses as a direct result of experiencing stressful events [26], yet physiological responses can also be activated and prolonged by thinking about the stressful events [25, 27-29]. This process is captured in the perseverative cognition (PC) hypothesis, which suggests that the negative relation between stress and health may be better explained when accounting for the mediating role of PC, such as worry [25]. Evidence supporting the association between PC, or conscious stress-representations, and stress-related physiological activity has been accumulating [31-34]. Recently, the PC hypothesis was extended with the suggestion that stress-representations may also be activated in the absence of awareness—in other words—unconsciously [38, 39]. These unconscious stress-representations in turn are theorized to explain a large part of the prolonged stress-related physiological activity [38, 39]. Evidence for the extended PC hypothesis is, however, limited and mostly indirect [32, 40-46, 57-61].

The main aim of this thesis was to find direct evidence for the extended PC hypothesis in real life. To put it differently, we aimed to examine whether (unconscious) PC can prolong physiological activity and increase subjective health complaints (SHC). To address this question, we first examined whether a short Internet-based worry-reduction intervention reduced conscious worry and improved SHC. Next, we set out to reduce both conscious and unconscious PC in primarily at risk individuals using (a) a smartphone-based worry-reduction intervention and (b) a subliminal evaluative conditioning (SEC) intervention. We examined the effect of the (unconscious) PC manipulations on health related parameters, thereby allowing us to draw conclusions about directionality and causality. In this final chapter we summarize and discuss the main findings from the included studies. Furthermore, we discuss the theoretical and clinical implications of the findings, the strengths and limitations, and we present directions for future studies.

OVERVIEW OF MAIN FINDINGS

In *Chapter 2* we examined whether there was a causal relation between conscious PC and self-reported SHC in the general adult population. To accomplish this we aimed to manipulate worry using a simple 6-day worry-postponement intervention that was previously found to be effective. In this intervention participants were instructed to notice their worries and to postpone these worries to a special 30-min worry period in the early evening. This was the first study to offer the worry-postponement intervention via the Internet, thereby making a simple and cost-effective intervention available to a larger community of self-labeled worriers. Data of 351 participants were included in the analyses. The cross-sectional findings showed that there was a positive association between worry and SHC, which replicated previous findings [25, 31, 33, 86, 88]. The experimental (or interventional) findings were, however, contrary to our expectation; that is, no support was found for the hypothesis that the intervention resulted in a larger decrease in trait and daily worry, SHC, or negative affect compared to participants in the control condition who simply registered their worries. Since the intervention was ineffective at reducing worry, we were unable to test whether reducing worry had a positive effect on (self-reported) health. Thus, in this study we failed to test if worry indeed caused SHC. This lack of effect may have been caused by participants' failure to become competent in postponing their worries within the intervention period. Only 24% of the participants who were instructed to postpone their worrying felt that their ability to do so was adequate. Considering the habitual nature of worrying, it is conceivable that individuals may require considerably more time and practice to replace their habit to worry with alternative ways of responding.

Ecological momentary interventions (EMIs) offer viable methods to promote treatment frequency in a relatively easy way to 'break' cognitive habits, such as worry. Not only are EMIs of interest because people can be trained *directly* when they experience complaints such as worry, but EMIs also allow individuals to practice repeatedly throughout the day, which may promote the effectiveness of the intervention [67, 265, 266]. These basic EMI characteristics are specifically of interest when aiming to break the habit to worry, because breaking non-adaptive habits can either be done by changing the environment that individuals are in (thereby removing the cue that initiates the habit) [267, 268] or by forming new responses in the existing environment [269, 270]. As it is virtually impossible to remove all cues that elicit an individual's habit to worry, it may be more effective to use an EMI to help an individual initiate and maintain more adaptive, alternative responses in the actual environment [271, 272]. Yet little is known about the effectiveness of EMIs. In *Chapter 3* we therefore systematically

assessed and meta-analyzed the effect of EMIs on mental health problems and positive psychological well-being. A small to medium effect of EMIs was found on mental health and the effect was not significantly different for anxiety, depression, perceived stress, or positive psychological outcomes. Larger effects—compared to stand-alone EMIs—were found when individuals received support from a mental health professional (MHP) in addition to the EMI. The findings must, however, be interpreted with caution considering (a) the low reported study quality, (b) the relatively small sample sizes, and (c) because the effect was smaller in between-subject studies compared to within-subject studies (and within-subject studies are at a greater risk for type-II errors). There is definitely a need for randomized controlled trials (RCTs) with an adequate number of participants to carefully examine the potential of EMIs. Still, the initial data suggests that EMIs are an easy and cost-effective strategy to improve mental health and positive psychological well-being in both healthy and clinical populations.

There is now evidence that EMIs can be used to improve mental health problems, but to date no study has examined whether EMIs can also be used to reduce (unconscious) PC and improve physiological health. It is theoretically plausible that EMIs can be specifically useful when attempting to break the habit to worry. As the EMI can serve as a direct reminder in daily life to display adaptive habit behavior [271, 273, 274] and—through repetition—can help to break the habit to worry [67, 265, 266]. In *Chapter 4* we report the findings of a pilot study using a daily worry-reduction EMI with mindfulness exercises. The main goal of the study was to examine the feasibility and preliminary effectiveness of the 4-week intervention that trained people repeatedly throughout the day to break the habit to worry. In terms of effectiveness we were particularly interested if this EMI could improve physiological indications of stress, namely HRV levels. For this purpose, high worrying students were randomized to either the worry-reduction EMI with mindfulness exercises or to an active-control condition that consisted of daily emotion registrations. The primary outcomes of interest of this pilot study were feasibility and ambulatory assessed HRV as marker of physiological stress responses. The training was feasible and participants completed on average 70% of all the training sessions. This suggests that offering five short and easy to complete training sessions per day was appropriate. Importantly, the training was easy to do, was taken seriously, and doing the training did not interfere significantly with the daily lives of the participants. Both the worry-reduction EMI and the emotion registration resulted in an increase in HRV from pre- to post-intervention. No effects were found on heart rate (HR), worry, anxiety, acceptance, and affect (both implicit and explicit). However, the effect sizes for trait worry and acceptance were small to medium and in the expected direction. These first findings showed that HRV improved

in individuals who received the worry-reduction intervention as well as in individuals who merely repeatedly registered their emotions. Yet only an effect was expected in the condition that received the worry-reduction intervention with mindfulness exercises. These findings could mean two different things. On the one hand, it could indicate that both strategies are effective in reducing physiological stress responses. On the other hand, it could mean that both interventions were ineffective. The observed HRV increase could have been caused by non-specific aspects of the design (e.g., due to an initial HRV decrease as a result of anticipation or novelty of the measurements) or the increase in HRV was simply a spurious finding possibly as a result of the small sample size. The latter could also have obscured a small superior effect of the worry-reduction intervention. To determine which of the explanations was legitimate, the EMI needed to be examined in another study including a no-treatment waitlist control condition (to test whether the interventions were effective and rule out the explanation of nonspecific effects) and a larger number of participants (to rule out spurious findings and to be able to detect relatively small differences between the two treatments).

To this end, a RCT was conducted and the findings are discussed in *Chapter 5.* The RCT was comparable to the pilot study, but now included a waitlist control condition and individuals with high levels of work stress were specifically targeted. Individuals with high levels of work stress were targeted, because these individuals are at risk to show physiological stress (i.e., low levels of HRV) and the chances of the worry-reduction intervention to impact HRV are therefore considered high. A total of 136 participants were randomized across the three conditions. The effect of the daily worry-reduction EMI with mindfulness exercises was examined on ambulatory assessed HRV and unconscious stress. The results showed—against our expectation—that the EMI did not have an effect on either HRV or unconscious stress. Additionally, exploratory analyses indicated that the EMI also did not affect HR, work stress, worry, anxiety, depression, or mindfulness. So, the EMI proved ineffective at improving the proposed mediators of the stress-health relationship, that is, worry and unconscious stress. Therefore, we were unable to test whether conscious and unconscious stress-representations caused physiological activity. Nevertheless, exploratory analyses—which are not reported—indicated that conscious stress-representations were associated with physiological activity. In line with previous studies (for a full overview, see [34]) and the PC hypothesis [25], we found that higher levels of state worry frequency and trait worry were associated with lower levels of HRV. However, in contrast with the extended PC hypothesis [38, 39], no significant associations were found between unconscious stress-representations and physiological activity.

In Chapter 6 we examined whether a direct manipulation of implicit mental

representations (of self-esteem)—which are indicative of unconscious stress—affected cardiovascular activity and reactivity to a stressor. Across three experiments we aimed to reduce automatic negative self-associations by repeatedly and subliminally coupling self-related words like 'I' to positive affective words like 'smart' (i.e., SEC). The first experiment was specifically set up as a replication of a study by Dijksterhuis [78] and examined whether SEC could be used to increase implicit self-esteem in the general student population. In Experiments 2 and 3 we examined whether such a self-esteem manipulation reduced cardiovascular (re)activity in high worrying students. In three experiments (with a total sample size of 242) we thoroughly tested the hypothesized effects of SEC. Notably, in *none* of the three experiments did we replicate the previously reported positive effects of SEC on self-esteem, despite using the same manipulation and procedure. In addition, no effects were found of SEC on unconscious stress—operationalized as implicit affect—and cardiovascular (re)activity. In this study we were thus unable to test whether an implicit mental representation (of self-esteem) had an effect on physiological activity, because implicit self-esteem was not significantly increased as a result of the manipulation. We did find that individuals with low levels of trait self-esteem had an increased cardiovascular reaction in response to the stressor (compared to individuals with high trait self-esteem). In contrast with the extended PC hypothesis, this stressor-induced increase in cardiovascular activity did not fluctuate with variations in implicit self-esteem. This sole finding is, however, insufficient to completely disregard the extended PC hypothesis, because it is based on exploratory analyses and addressed only one possible operationalization of unconscious stress.

IMPLICATIONS

Theoretical Implications

In this thesis we aimed to manipulate conscious PC (*Chapter 2*) and unconscious PC (*Chapters 4-6*) to examine whether such manipulations would affect health-related parameters in the laboratory and in daily life. It was our intention to manipulate these stress-representations, because it would allow us to draw conclusions about causality and directionality. Throughout this thesis, however, we were unsuccessful in manipulating both conscious and unconscious PC, and therefore we were unable to examine the effect of such manipulations on health-related parameters. Thus, we failed to find direct proof for the extended PC hypothesis in daily life.

Partial support for the PC hypothesis was, however, found in *Chapter 2*. In line with previous studies [25, 31, 33, 86, 88], we found that individuals with higher levels of trait worry had higher levels of SHC at baseline. Yet this evidence is cross-

sectional and so we cannot be sure that worry caused SHC or that experiencing SHC caused individuals to worry. Notably, this association was not independent of negative affect (meaning that the positive association disappeared after controlling for a persons' negative affectivity). A related finding is reported by Thomsen et al. [275], who showed that the association between rumination and self-reported health in the elderly population was mediated by negative affect, specifically, sadness. This could suggest that repetitive thinking caused or prolonged negative affective states, which in turn resulted in decreased health. However, the association between PC and health-related parameters was not always mediated or fully mediated by negative affect [88, 276-281]. It is currently unclear what caused these differences in findings. Differences in study population could potentially have caused the divergent findings, although this would require further investigation. The results were thus mixed and no firm conclusions can be drawn on the unique contribution of PC in the association with health-related parameters.

Stronger evidence for the PC hypothesis comes from prospective data and in *Chapter 2* we additionally show that, in the control condition (in which participants did not receive an intervention), daily worry on the first three registration days was prospectively related to SHC at post-intervention. This suggests that worry is indeed a risk factor for experiencing SHC and this lends support for the PC hypothesis (i.e., finding is in line with previous studies [86, 88, 275, 282, 283]). This relation, however, was again not independent of negative affect. Although the latter is in contrast with prospective data of most available studies [86, 88, 275, 282, 283], it does correspond to an observation that the effect of a worry-reduction intervention on SHC was no longer significant after controlling for negative affect at baseline—potentially indicating that the relation between PC and SHC is influenced or moderated by a persons' negative affectivity [86]. In *Chapters 2, 4, 5,* and *6* we were unfortunately unable to examine whether the effect of a worry-reduction intervention on health was independent of negative effect, because the described interventions failed to change (unconscious) PC. Therefore, it remains uncertain whether PC are directly related to health (independent of negative affect) and, more importantly, whether reductions in PC can improve health. Not only is there a limited evidence base to draw conclusions from, but the conclusions from the present and previous studies are further limited due to differences in the operationalization of PC (e.g., trait worry, state worry, modern health worries) and negative affect (e.g., negative affect, trait anxiety). These operational differences may explain the mixed findings, considering that a review by Brosschot, Gerin, and Thayer [25] concluded that trait worry was more consistently associated with health outcomes. There is thus clearly a need for more studies that examine whether the act

of worrying itself affects health or whether it is merely the experience of negative affect or distress. Even though PC and negative affect are thought to be associated [81, 284], it is important to determine the unique contribution of each individual feature as this information can help to guide intervention development.

The interventions thus failed to reduce both conscious and unconscious stress-representations, which were proposed to mediate the effect on health-related outcomes. Still, even though the proposed mediators were not affected, a positive effect of the worry-reduction intervention with mindfulness exercises could have been expected. To explain, there is evidence that health benefits can occur as a result of mindfulness-based practice [206, 207, 285, 286], potentially through different mediating pathways [202]. Mindfulness-based practice, through improved attentional control and emotional regulation, has been shown to impact other CVD risk factors such as physical activity and diet (i.e., for a detailed discussion, see [202]). So, a positive effect of the intervention on health-related parameters could have emerged despite the lack of change in conscious and unconscious stress-representations. Nevertheless, contrary to previous findings [206, 207, 285, 286], no such effects were observed in this thesis.

Obviously, the fact that we were unable to find evidence for the extended PC hypothesis does not confirm the null hypothesis that there is no association between (un)conscious stress and health. The absence of change in unconscious stress-representations is likely due to the use of manipulations that were insufficient or too mild, especially for a highly stressed sample, or due to an unsuccessful implementation of the manipulations in the sample. Moreover, with respect to assessing unconscious stress, the instruments that were used may have limited construct validity and assessed only some of the possible operationalizations of unconscious stress [38]. To our knowledge, there were no evidence-based interventions available for reducing both conscious and unconscious stress-representations. Therefore, we selected elements that were theoretically most likely to affect these stress-representations. We specifically reasoned that frequent daily repetition was important. Thus, intervention components were selected that could be easily and repeatedly implemented in daily life. Nevertheless, both the 6-day Internet-based worry-postponement intervention and the 4-week smartphone-based worry-reduction intervention with mindfulness exercises proofed to be unsuccessful. The inefficacy could have been due to the length of the training (sessions). As described in *Chapter 2*, the 6-day intervention period may not have been long or strong enough for participants to learn how to postpone their worries. Therefore the intervention period was elongated and the number of daily training sessions was increased in *Chapters 4* and *5*. Still, the length of the actual daily training sessions may have been too short to improve stress-representations. Even though a

review found that the overall length of mindfulness trainings was not associated with the size of the effect on psychological distress, the average duration of the weekly training sessions—across the included studies in the review—was quite high (i.e., 121 min) [287]. Therefore, these results do not directly translate to our training, which was considerably shorter (i.e., 7 min on average per training session in *Chapter 5*). To fully learn the principles of mindfulness-based practice it is conceivable that individuals require longer exercises. The length of the training sessions may have been especially problematic in combination with the unstructured format of the training. To explain, individuals were at liberty to choose which of the mindfulness exercises they wished to do and there were no rules governing the sequence of exercises. We specifically choose this strategy, because it would allow individuals to tailor the intervention to their own needs (e.g., choose exercises that fit with their mental and physical state) and environment (e.g., choose exercises that fit with their time schedule). In order for the intervention to be effective it may, however, be necessary to offer individuals explicit guidance on how to get started by providing guidelines on what exercises to do and in what order. Indeed, the formal curriculum of mindfulness based stress reduction programs are structured [187] and these programs are known to be effective [115, 186, 288]. Furthermore, the majority of the mindfulness-based EMIs that were discussed in *Chapter 3* used a structured approach and found positive effects of the intervention on mental health problems. Together, this suggests that a step-by-step, structured approach is worthwhile to consider in future studies. Such an approach can help individuals to fully learn to focus on the present moment and thereby break the habit to worry. Our findings do not refute the importance of daily practice, but they do indicate that future studies should carefully reconsider both the content and the intensity of the intervention. All in all, throughout this thesis we were unsuccessful in examining whether unconscious stress-representations affected health-related parameters, because we failed to manipulate stress-representations. Clearly more studies are needed to determine the validity of the extended PC hypothesis in daily life.

Clinical Implications

Stress and mental health problems are highly prevalent, but access to mental health care to deal with these experiences is limited in both low-income countries and high-income countries including the Netherlands [119, 129, 289]. A dose-response relation exists between the severity of the mental health problems and the use of mental health services [289]. Nevertheless, half of the individuals with severe mental health problems in the Netherlands are not receiving treatment and the numbers are even more concerning for other countries [289]. These findings are likely the result of health care

budgets that are insufficient given the scope and severity of mental health problems [290]. Still, the finding is perplexing when considering that individuals with mild symptoms and even those without apparent disorders are receiving treatment [289]. Altogether, it suggests two things: (a) access to care needs to be improved and (b) care must be correctly allocated to those most in need. Mobile technologies, like EMIs, may be used to address both objectives. To explain, the number of mobile phone users is large and continues to increase [291, 292], so interventions using mobile technology can have a universal reach [124, 293]. Plus, such interventions may be especially useful to treat the 'worried well' and those with mild symptoms [179], thereby freeing resources for individuals with more severe complaints. EMIs can thus be of immense importance for clinical practice and may provide a new way to address deficiencies in health care. This may seem as an ideal future perspective, but we are not there yet as there is limited research on the effectiveness and implementation of such self-management interventions [124, 292].

In *Chapter 3* we took an important first step; that is, we summarized what is known so far on EMIs and we examined the overall effectiveness. All in all, the evidence suggested that EMIs can be used to improve mental health problems and positive psychological well-being. Even though offering an EMI offers the advantage of anonymity and autonomy, receiving some form of guidance does lead to larger effects compared to stand-alone EMIs. This additional help may in turn also stimulate adherence to the intervention, which is likely to further increase the effectiveness. In light of the possibility of offering mental health care using mobile technology, these findings are of paramount importance. However, the number of studies—and thus EMIs—that could be included in the analyses was small, especially when compared to the number of health self-management apps that are available in different app stores (i.e., for depression alone there are over 1500 apps available) [294]. There is thus a massive discrepancy between availability of EMIs and their evaluation. On the rare occasion that an EMI was evaluated, this was often done in small samples thereby limiting definitive conclusions regarding effectiveness. In *Chapters 4* and *5* we add to the limited scientific evidence base by examining the feasibility of our developed EMI in a pilot study and the effectiveness in a large-scaled RCT. As discussed, the stand-alone worry-reduction EMI with mindfulness exercises appeared to be feasible and was taken seriously, although adherence to the training sessions could have been higher in the RCT (i.e., only 63% of all daily training sessions was completed). Despite the fact that the EMI was well received, the null results indicated that it is not beneficial to implement this particular EMI in a population suffering from work stress. More well-designed RCTs and replications of such RCTs are needed to confirm the potential of

EMIs in mental health care, and careful attention should also be paid to potential risks.

In *Chapter 4* and *5* we examined the efficacy of an EMI that used both a worry-reduction intervention and mindfulness exercises. The worry-reduction intervention was ineffective in reducing conscious worry in *Chapter 2*, yet positive effects of this intervention on conscious worry had previously been found [86-89]. We reasoned that a longer intervention period with frequent daily practice and additional mindfulness exercises—which is known to be an effective intervention component [117, 201, 295]—would proof to be more potent in reducing PC. However, the combination of the worry-reduction intervention with mindfulness exercises was not successful in reducing PC in *Chapter 4* and *5*. When interpreting these results it is important to consider that the two intervention components had not been combined before and that the intervention was offered using a new methodology, that is, on a smartphone in daily life. This could imply two things. First, it could indicate that the combination of change- and acceptance-based intervention components was ineffective. Second, it could mean that the combination in principle could be effective in reducing (unconscious) PC, but that the EMI format was unsuitable to effectively deliver the intervention. It remains to be investigated which of the two options is correct. Considering the advantages of EMIs for delivering short and cost-effective interventions, it would be worthwhile to examine the efficacy of an EMI using either worry-reduction or mindfulness (and to compare the effectiveness of the two EMIs). Additionally, it is important to determine whether an EMI format is acceptable when aiming to break the habit to worry. An elaborate cross-over design with different interventions and delivery modalities could be used to answer these questions. In this endeavor it would also be valuable to study the added value of including additional support from a mental health professional to the EMI protocol (for example, to stimulate adherence to the intervention or to check progress). Naturally, support will make an intervention less cost-effective compared to stand-alone EMIs, but support can come in different gradations. Some studies have for example provided a treatment package including both an EMI and face-to-face therapy (e.g., [144, 145, 163, 175]), whereas Watts et al. [167] only provided support at the start of the EMI and other authors have only provided feedback on homework assignments [161, 166]. The type of support thus differs greatly and intervention developers can aim to achieve the most optimal balance between costs and effectiveness. Importantly, conclusive evidence that support is a necessity for all individuals is lacking and it could be that individuals with lower levels of symptoms do not need support at all. It might be useful for future studies on EMIs to include two intervention groups, one with support and one without, thereby providing more concrete evidence on the role of support in EMIs. Psychology students could be considered for an affordable delivery of support,

considering that individuals with limited professional training experience can achieve successful therapeutic change (just like professionals) [296, 297].

Furthermore, in this thesis we found no evidence that SEC could be effectively used as a short intervention to reduce unconscious stress. Considering that no effect of SEC was found in a highly controlled laboratory environment, we did not pursue to explore the usefulness of SEC in daily life. We were thus unable to reproduce previously reported positive SEC effects. It is not the first time that promising effects could not be reproduced [298, 299]. In a shared effort to determine the reproducibility of psychological science, it was indeed found that only 36% of the replication studies had significant results compared to 97% of the original studies [299]. Moreover, the effect sizes were considerably smaller in the replication studies. This underscores the importance of conducting replication studies.

STRENGHTS AND LIMITATIONS

A strength of this thesis is that we aimed to examine the validity of the extended PC hypothesis in daily life using a well-designed, pre-registered, and adequately powered randomized controlled design. This design—if the manipulations had been effective—would have allowed us to make statements about causality and this would have supplemented the mostly indirect evidence base for the extended PC hypothesis [32, 40-46, 57-61]. Furthermore, individuals were studied in their real life situations and we thereby intended to do justice to the complexity of human beings and "capture life as it is lived" [71, 300, p. 580]. Traditional assessment strategies—like retrospective self-report questionnaires—provide useful information, but the method is insensitive to variations in actual behavior during the day and this can be assessed using ecological momentary assessments [301, 302]. Moreover, the in-time assessment of individuals' yielded data that was less influenced by recall bias and more ecologically valid compared to laboratory studies.

A related strength is that we assessed physiological activity in daily life and not in a laboratory-based setting. Even though physiological activity can be assessed reliably and relatively easily in the laboratory with few artifacts due to movement or technical problems, the physiological data that is collected in this highly controlled environment may not translate well to real world functioning [63, 64]. For instance, it was shown that a stressor in daily life—that was personally relevant to the individual—elicited a far greater physiological response compared to five different commonly used laboratory stressors [64]. Ambulatory assessment of physiological activity may thus more accurately reflect how an individual experiences stressful events in ones' life. The

need for ambulatory assessment in the field of psychology is now increasingly being recognized, as evidenced by a special section on the topic in European Psychologist (2009, volume 14, issue 2), a special issue in European Journal of Psychological Assessment (2007, volume 23, issue 4), and with the publication of a handbook describing different research methods in daily life [71].

Other strengths of the reported studies include (a) the use of different techniques to manipulate PC, (b) our examination of the PC manipulations on different outcome measures, namely, explicit and implicit measures, and physiological activity, and (c) our focus on clinically relevant populations that were at risk for experiencing high levels of (unconscious) stress.

One clear limitation of the research in this thesis is that the different PC manipulations failed to change (unconscious) PC and therefore we were unable to examine the possible impact of such manipulations on health. The results thus do not provide conclusive evidence on whether (unconscious) stress-representations directly affect health. Of course the interventions are not only a manipulation of stress-representations and the mindfulness exercises, for instance, can be expected to have effects on health-related parameters through other mediators (e.g., [202]). Identifying mediators or mechanisms through which the intervention can have its effect on health is one way to advance an effective delivery of psychological treatments [182, 303]. In *Chapter 2* we were able to show that PC was prospectively related to self-reported health, but the cause-effect relation between stress-representations and health remains to be determined in future studies.

The second limitation has to do with the methodological difficulties in measuring unconscious or automatic processes. In the present thesis we specifically aimed to assess unconscious stress-representations and we set out to measure this using two different strategies. An affect misattribution paradigm was used (i.e., Implicit Positive and Negative Affect Test [IPANAT]; *Chapters 4-7*) and a measure that is based on automatic attitude activation (i.e., Implicit Association Test [IAT]; *Chapters 5-6*). However, measuring implicit processes is sometimes met with understandable skepticism, raising questions about what such measures represent and whether they are truly measuring what they set out to measure. These discussions fuelled research examining the psychometric qualities of implicit measures and in this endeavor the IAT has received the most attention [304, 305]. Current reviews and meta-analyses suggest that the reliability (both internal consistency and test-retest reliability) and predictive validity of the IAT are acceptable [221, 305, 306]. Yet the findings are mixed for the relation between the IAT and other implicit or explicit measures that attempt to measure the same construct [220, 304-306]. Notably, stronger associations with other implicit

measures emerged after accounting for measurement error [307]. Less psychometric evidence is available for the IPANAT, but a recent review discussed promising evidence [308]. Considering the importance of using reliable assessment strategies for testing hypotheses, more psychometric research is definitely needed. Although there is initial evidence suggesting that implicit processes can be reliably assessed, future studies should attempt to explain the mixed findings so that more firm conclusions can be drawn on the usefulness of current implicit measures.

FUTURE DIRECTIONS

Obviously, as the extended PC hypothesis remains untested, there is a clear opportunity for future research to further examine the validity of a causal relationship between (unconscious) stress-representations and health. Considering the necessity of a reliable PC manipulation for testing the hypothesis, we recommend researchers to carefully review the manipulation of interest and to be attentive that previously reported positive effects cannot always be replicated [299]. Indeed, in *Chapter 2* we were unable to replicate previously reported positive effects of the worry-postponement intervention [86-88] and in *Chapter 6* we failed to find evidence for the efficacy of SEC, which was in contrast with previous reports [78, 79]. Our studies highlight the importance of performing such replications. For instance, based on the null results reported in *Chapter 2*, we were able to adjust the PC manipulation. Specifically, we devised a more comprehensive strategy to manipulate PC in daily life: we (pilot) tested the strategy in *Chapter 4* and implemented it in *Chapter 5*. Against expectations, this strategy was also not effective for manipulating PC. Considering the complexity and habitual nature of PC it might be difficult to find a reliable PC manipulation (especially in daily life). Future studies could also consider testing the hypothesis in individuals with generalized anxiety disorder—a disorder that is characterized by excessive worrying—who are about to undergo an evidence-based psychological treatment for their complaints. It has been shown that cognitive therapy (targeting worry) can reduce anxiety, depression, and worry (e.g., [309-311]); however, such findings do not provide evidence that the change in worry was directly responsible for the change in anxiety and depression. One treatment study, in individuals with generalized anxiety disorder, has shown that an early reduction in conscious PC predicted further treatment responses [312]. Furthermore, a systematic review by van der Velden et al. [313] found some evidence that conscious PC mediated the effect of mindfulness-based cognitive therapy in individuals with depression. These initial findings are interesting, but there is definitely need for more meditational studies that examine whether the change in

worry caused the change in outcome variables. These studies can help advance our understanding of the mechanisms that cause the treatment effect and can thus help us understand why treatments are effective [182, 303]. To identify potential mediators, studies should assess the proposed mediator(s) and outcome variables before, during, and after the treatment. Assessment of mediators and outcome variables *during* the treatment is not always done, but this is necessary to identify the timeline of change in the study variables [182]. So, to examine whether changes in (unconscious) PC are related to changes in health, it is necessary to assess (unconscious) PC and health-related parameters at least before, during, and after the intervention.

In *Chapter 3* we found that EMIs can be used to improve mental health, but in *Chapters 4* and *5* we found no evidence supporting the use of our developed EMI. In this regard, several potential avenues for future research have already been mentioned above that might lead to more effective PC manipulations (e.g., increasing length of training sessions, offering a structured training). In addition, with regard to EMI characteristics, little is known about what works or what works for whom and this provides ample opportunities for future research. As an illustration, the EMI that was tested in *Chapters 4* and *5* was randomly scheduled throughout the day. Alternatively, training sessions could be scheduled in accordance with the individual. Flexibly scheduling could be applied to both the number of training sessions and the timing. For example, on a workday an individual might prefer to do one training session in the evening, whereas on a non-work day an individual might prefer to complete multiple training sessions throughout the day. In the same way it could be possible to take the duration of training sessions into account. By allowing an individuals' preference to shape the EMI, both the adherence to and the satisfaction with the training might actually increase while preserving the advantage of training people in their daily lives. Adopting this strategy would be in line with Internet-based interventions whereby individuals typically log onto a website to receive their training when it is convenient for them and these types of interventions have been found to be effective for a number of disorders [70]. Employing such a strategy would allow an individual to train in daily life, but you might loose the advantage of training people when it matters, that is, in stressful or worrisome situations. Therefore other strategies to promote adherence can also be considered: providing incentives [314], using motivational interviewing [315], providing progress reports to participants (which in turn could also be used to detect non-responders) [316], or using gamification to increase user engagement [317].

When developing new EMIs it is recommended to involve the end-user, because these individuals are to use the intervention and their input will likely improve the acceptability, implementation, and effectiveness of the actual intervention [124,

293]. Recently, tools and guidelines have become available to aid the development and evaluation of EMIs. Olff [124] for instance provided a checklist with different issues that need to be addressed when developing an evidence-based EMI and Whittaker, Merry, Dorey, and Maddison [318] delineated a six-step process for researchers to guide the development and testing of EMIs. This process consists of (a) conceptualization (or intervention mapping), (b) formative research consisting of focus groups or online surveys with the target population to guide the EMI development, (c) pretesting the intervention content, (d) a small pilot study in the target population, (e) a RCT, and (f) a qualitative follow-up to determine how the EMI or the implementation can be improved. These steps are expected to result in a potent intervention, but a clear disadvantage to this approach is the immense time investment. Consequently, the technology behind the EMI may already be outdated by the time the EMI has been fully developed and tested. Importantly, in this period distinct changes may also have emerged in the way people use such technology and this could possibly affect the appropriateness of the EMI [293, 318]. To speed up the development and evaluation other approaches can be considered as well like the Multiphase Optimization Strategy [319]. The strategy—that was specifically developed for eHealth interventions—describes how factorial designs can be used to identify both the most effective intervention components and the optimal dosage of the components before testing the complete intervention in a RCT. The RCT is still the preferred design for testing the effectiveness of the EMI, yet it may not always be practical. In that event other designs can be considered, for instance, an interrupted time series design, a multiple baseline design, or a controlled pre-post design (see [320]). All in all, for researchers it will be necessary to find an appropriate balance between developmental speed and scientific evaluation.

CONCLUSIONS

The studies in this thesis examined the validity of the (extended) PC hypothesis in daily life in at risk individuals. All in all, we failed to find direct support for the hypothesis that (unconscious) PC affects health-related parameters [38, 39]. However, this may be because we failed to adequately manipulate PC and therefore we were unable to examine whether changes in PC were related to changes in health. There is thus need for future studies that use different techniques to manipulate (unconscious) PC, so that the effect on health-related parameters can be studied. Our findings do not support the use of the Internet-based worry-reduction intervention for improving PC and SHC. Yet evidence was found that EMIs can be used to train people during the day and that such interventions can improve mental health. Nevertheless, the EMI that was investigated

in this thesis was considered ineffective and there is definitely room for future studies to carefully determine what works for whom. Moreover, no evidence was found that SEC had a positive effect on unconscious stress or physiological activity. Considering the high prevalence of stress, it is important that researchers focus on gaining a more complete understanding of how stress negatively affects health.

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Nederlandse samenvatting

Stress komt veel voor in de huidige samenleving en dit is zorgwekkend aangezien onderzoek herhaaldelijk heeft aangetoond dat het ervaren van stress een negatieve invloed heeft op de lichamelijke gezondheid [11-17]. Zo vergroot stress bijvoorbeeld de kans op hart- en vaatziekten [18-24]. Het negatieve effect van stress op de gezondheid is het resultaat van de fysiologische activiteit, die wordt geactiveerd tijdens of voorafgaand aan de stressvolle gebeurtenis en (langdurig) verhoogd blijft na afloop van de stressvolle gebeurtenis [10, 12, 25]. Wanneer mensen iets stressvols meemaken slaat hun hart in een minder variabel ritme en als deze hartslagvariabiliteit langdurig verlaagd blijft zou dit uiteindelijk een negatief effect kunnen hebben op de lichamelijke gezondheid [36]. Het gros van de onderzoeken naar de fysieke gevolgen van stress heeft zich tot op heden gericht op de fysiologische activiteit tijdens het meemaken van stressvolle gebeurtenissen [26]. Echter, de fysiologische activiteit kan ook geactiveerd en verlengd worden door het nadenken, piekeren, over (mogelijke) stressvolle gebeurtenissen [25, 27-29]. De perseveratieve cognitie hypothese suggereert daarom dat de negatieve relatie tussen stress en gezondheid beter verklaard kan worden wanneer er rekening wordt gehouden met de (mediërende) rol van perseveratieve cognities, zoals piekeren [25]. Diverse onderzoeken laten inmiddels zien dat er een associatie is tussen perseveratieve cognities, ofwel bewuste stress-representaties, en stress-gerelateerde fysiologische activiteit [31-34]. Recentelijk is de perseveratieve cognitie hypothese uitgebreid met het idee dat de stress-representaties ook geactiveerd kunnen zijn buiten het bewustzijn om, met andere woorden, onbewust [38, 39]. Deze onbewuste stress-representaties zouden mogelijk een groot deel van de langdurige stress-gerelateerde fysiologische activiteit kunnen verklaren [38, 39]. Uit een eerdere studie blijkt bijvoorbeeld dat het meemaken van een stressvolle gebeurtenis gedurende de dag invloed heeft op de hartactiviteit en dit effect houdt aan tijdens de slaap, een periode waarin niet bewust gepiekerd kan worden [40]. Een andere studie heeft daarnaast aangetoond dat bewust piekeren hartactiviteit verhoogd en zelfs 2 uur later nog verhoogd was terwijl het piekeren al was gestopt [32]. Mogelijk verklaren onbewuste stress-representaties deze langdurige activiteit. Bewijs voor de uitgebreide perseveratieve cognitie hypothese is echter beperkt en voornamelijk indirect [32, 40-46, 57-61].

Het doel van dit promotieonderzoek was om direct bewijs te vinden voor de uitgebreide perseveratieve cognitie hypothese in het dagelijks leven. We hebben in verschillende studies onderzocht of (onbewuste) perseveratieve cognities inderdaad van invloed zijn op fysiologische activiteit en zelf gerapporteerde lichamelijke gezondheid. Om dit te onderzoeken hebben we eerst gekeken of een korte, online piekerinterventie zorgde voor een vermindering in bewust piekeren en een verbetering

van zelf gerapporteerde lichamelijke gezondheid. Daarnaast hebben we geprobeerd om bewuste en onbewuste perseveratieve cognities te verminderen met behulp van (a) een piekerinterventie die werd aangeboden op de mobiele telefoon en (b) een subliminale evaluatieve conditionering interventie. Meer direct bewijs voor de uitgebreide perseveratieve cognitie hypothese zou worden geleverd als deze manipulaties van (onbewuste) perseveratieve cognities gepaard zouden gaan met een vermindering van stress-gerelateerde lichamelijke activiteit en een verbetering van zelf gerapporteerde gezondheid. Hieronder worden de belangrijkste bevindingen besproken.

BELANGRIJKSTE BEVINDINGEN

In *Hoofdstuk 2* hebben we onderzocht of bewust piekeren een negatieve invloed had op zelf gerapporteerde lichamelijke gezondheid. Om dit te onderzoeken hebben wij geprobeerd het piekeren te verminderen met behulp van een piekerinterventie en hebben wij onderzocht of deze vermindering in piekergedachten een positief effect had op zelf-gerapporteerde lichamelijke klachten. De interventie bestond uit het leren opschorten en uitstellen van piekergedachten en eerdere onderzoeken lieten zien dat deze methode effectief is in het verminderen van piekeren en het verbeteren van zelf-gerapporteerde gezondheid [81, 82, 125]. In deze studie werd de interventie voor het eerst aangeboden via het Internet en hierdoor werd een simpele en kosteneffectieve interventie beschikbaar voor een grote groep mensen uit de algemene bevolking. In totaal hebben 996 mensen, uit de algemene bevolking, zich aangemeld voor deelname aan het onderzoek (maar niet alle geïnteresseerde deelnemers hebben het onderzoek volledig afgemaakt). Alle aangemelde deelnemers werden willekeurig verdeeld over twee groepen. Beide groepen registreerden gedurende 6 dagen hoe vaak ze piekergedachten hadden en hoe lang deze gedachten duurden. Mensen in de interventiegroep kregen daarnaast de instructie om hun piekergedachten uit te stellen naar een dagelijks piekerhalfuur. Het onderzoek is afgerond door 351 mensen en in deze groep vonden we een positieve associatie tussen piekeren en lichamelijke klachten voor aanvang van de behandeling. Met andere woorden, mensen die meer piekergedachten hadden rapporteerden ook meer lichamelijke klachten. Deze bevinding was in lijn met eerdere studies [25, 31, 33, 81, 82]. Echter, in tegenstelling tot onze verwachting, zorgde de piekerinterventie niet voor een vermindering van piekergedachten of lichamelijke klachten (in vergelijking met de groep die enkel piekergedachten registreerden). De interventie had dus geen invloed op piekeren en daardoor konden we niet onderzoeken of een vermindering van piekergedachten een positief effect had op (zelf-gerapporteerde) lichamelijke gezondheid. De interventie

was mogelijk ineffectief, omdat deelnemers moeite hadden met het uitstellen van hun piekergedachten. Slechts 24% van de deelnemers was in staat om, gedurende de interventie periode van 6 dagen, het piekeren uit te stellen naar het dagelijkse piekerhalfuur. Mogelijk hebben mensen, gezien de habituele aard van piekeren, meer tijd en oefening nodig om de gewoonte van piekeren te vervangen door ander gedrag.

In *Hoofdstuk 3* nemen we 'ecological momentary interventions' ofwel EMIs onder de loep. De Engelse term EMIs verwijst naar interventies die worden aangeboden in het dagelijks leven met behulp van elektronische apparaten, zoals mobiele telefoons. Met behulp van EMIs kunnen mensen vaker getraind worden op een relatief eenvoudige manier. Een piekerinterventie aanbieden op de mobiele telefoon heeft twee duidelijke voordelen. Ten eerste, kunnen mensen *direct getraind* worden wanneer ze piekergedachten ervaren. Ten tweede, kunnen mensen *herhaaldelijk getraind* worden gedurende de dag en dit kan de effectiviteit van de interventie vergroten [67, 83, 84]. Deze twee EMI kenmerken zijn relevant voor het doorbreken van de gewoonte om te piekeren, omdat ongewenste gewoonten doorbroken kunnen worden door de directe omgeving van het individu te veranderen (waardoor de omgevingsprikkel, die normaliter het gewoonte gedrag activeert, verdwijnt) [85, 86] of door nieuw adaptief gedrag aan te leren in de huidige omgeving [87, 88]. Het is vrijwel onmogelijk om alle omgevingsprikkels te verwijderen die mensen aanzetten om te piekeren en het is daarom mogelijk effectiever om EMIs in te zetten voor het aanleren van adaptieve alternatieve gedragspatronen in de huidige omgeving [89, 90]. Er is echter nog weinig bekend over de effectiviteit van EMIs. Om hier inzicht in te krijgen hebben wij, in *Hoofdstuk 3,* een systematisch literatuuronderzoek en meta-analyse uitgevoerd. In totaal werden 33 studies meegenomen (n = 1301). Deze individuele studies onderzochten of een EMI effectief kan zijn in het verminderen van psychische klachten en het verbeteren van positief psychologisch welzijn. De samengevoegde resultaten van deze studies lieten zien dat EMIs kleine tot gemiddeld grote effecten hadden op psychische klachten. Er is daarnaast onderzocht of de grootte van het effect van de EMIs verschillend was voor de verschillende soorten psychische klachten. De gevonden positieve effecten bleken even groot voor angstklachten, depressieve klachten, ervaren stress en positief psychologisch welzijn. Een EMI was wel effectiever wanneer een individu extra ondersteuning ontving van een gezondheidszorg professional. De gevonden resultaten moeten echter wel met voorzichtigheid geïnterpreteerd worden, onder andere omdat (a) de gerapporteerde kwaliteit van de geïncludeerde studies laag was en (b) de onderzoeken relatief weinig deelnemers hadden. De effectiviteit van mobiele interventies moet verder onderzocht worden met behulp van gerandomiseerde en gecontroleerde studies met voldoende deelnemers. Desalniettemin suggereert de

initiële data dat mobiele interventies een gemakkelijke en kosteneffectieve manier zijn om psychische klachten te verminderen en positief psychologisch welzijn te vergroten in zowel klinische als gezonde groepen.

Er is nu bewijs dat EMIs gebruikt kunnen worden om psychische gezondheid te bevorderen, maar er is nog geen bewijs dat EMIs ook ingezet kunnen worden om (onbewuste) perseveratieve cognities te verminderen en lichamelijke gezondheid te verbeteren. In *Hoofdstuk 4* bespreken wij de bevindingen van een pilotstudie ter verkenning van de haalbaarheid en effectiviteit van een piekerinterventie met mindfulness oefeningen. De 4 weken durende interventie werd aangeboden op de mobiele telefoon en mensen werden herhaaldelijk gedurende de dag getraind om de gewoonte van piekeren te doorbreken. We waren specifiek geïnteresseerd of de EMI een positief effect had op een lichamelijke indicator van stress, namelijk hartslagvariabiliteit. Om dit te onderzoeken werden 26 studenten, die de neiging hadden om veel te piekeren zoals gescreend met een vragenlijst, willekeurig toegewezen aan de experimentele (n = 11) of actieve controle conditie (n = 15). Deelnemers in de experimentele conditie kregen de piekerinterventie aangevuld met mindfulness oefeningen aangeboden en deelnemers in de actieve controle conditie werden geïnstrueerd om dagelijks, meermaals, hun emoties te registreren. Resultaten lieten zien dat de training haalbaar was en dat gemiddeld 70% van alle aangeboden oefeningen in deze groep gedaan werd. Het aanbieden van vijf korte en gemakkelijke oefeningen per dag bleek dus haalbaar te zijn. Daarnaast werd door de deelnemers aangegeven dat de training eenvoudig was om uit te voeren, serieus werd genomen en dat het volgen van de training geen negatieve invloed had op het dagelijks leven. Na afloop van de interventieperiode was er een verbetering te zien in hartslagvariabiliteit in beide groepen (dus in zowel de groep met de piekerinterventie *met* mindfulness oefeningen als in de emotieregistratie groep). Een verbetering van hartslagvariabiliteit werd echter enkel verwacht in individuen die de piekerinterventie met mindfulness oefeningen hadden ontvangen. Dit zou kunnen betekenen dat beide interventies effectief waren (dus zowel de piekerinterventie met mindfulness oefeningen als de emotieregistratie). Het zou echter ook kunnen betekenen dat beide interventies niet effectief waren. Zo zou de geobserveerde verbetering in hartslagvariabiliteit bijvoorbeeld een toevalsbevinding kunnen zijn als gevolg van de kleine groep deelnemers. Bovendien ontbrak er in deze studie een zogeheten wachtlijst-controleconditie en deze conditie is belangrijk om uit te sluiten dat een waargenomen effect—in dit geval de verbetering in hartslagvariabiliteit—niet het resultaat is van spontane veranderingen (door bijvoorbeeld het verstrijken van tijd).

Om meer duidelijkheid te krijgen over de effectiviteit van de piekerinterventie hebben wij een gerandomiseerd en gecontroleerd onderzoek uitgevoerd met een

wachtlijst-controleconditie en een grotere groep deelnemers. Het onderzoek wordt besproken in *Hoofdstuk 5*. Het onderzoek is uitgevoerd bij mensen die werkstress ervaren, gemeten aan de hand van een vragenlijst, omdat deze individuen een verhoogd risico hebben om lichamelijke stress te ervaren (namelijk lage hartslagvariabiliteit). De piekerinterventie heeft hierdoor een grote kans om effect te hebben op hartslagvariabiliteit. De 136 deelnemers werden willekeurig verdeeld over de experimentele (n = 46), controle (n = 48) en wachtlijstconditie (n = 42). Het effect van de piekerinterventie met mindfulness oefeningen werd onderzocht op ambulant gemeten hartslagvariabiliteit en onbewuste stress. In tegenstelling tot onze verwachting, lieten de resultaten zien dat de interventie in deze studie geen effect had op hartslagvariabiliteit of onbewuste stress. Exploratieve analyses lieten daarnaast zien dat de interventie ook geen effect had op hartslag, werkstress, piekeren, angst, depressie en mindfulness. De EMI had dus geen positief effect op piekeren en onbewuste stress, de voorgestelde mediatoren in de relatie tussen stress en gezondheid. Hierdoor konden wij niet onderzoeken of bewuste en onbewuste stress-representaties van invloed waren op fysiologische activiteit. Desondanks lieten exploratieve analyses zien dat bewuste stress-representaties geassocieerd waren met gelijktijdig gemeten fysiologische activiteit. Net als eerdere studies (zie [34]) en in lijn met de perseveratieve cognitie hypothese [25] vonden we een lagere hartslagvariabiliteit bij mensen die veel piekerden. Er werd echter geen significante verband gevonden tussen onbewuste stress-representaties en fysiologische activiteit (in tegenspraak met de uitgebreide perseveratieve cognitie hypothese [38, 39]).

In *Hoofdstuk 6* hebben we onderzocht of een directe manipulatie van impliciete mentale representaties van laag zelfvertrouwen—wat als indicatief werd beschouwd voor onbewuste stress—invloed heeft op hartactiviteit in rust, en op de activiteit van het hart tijdens en na het meemaken van een stressvolle gebeurtenis (hart*re*activiteit). In drie experimenten was het doel deze automatische negatieve zelf-associaties te verminderen door herhaaldelijk zelf gerelateerde woorden (bijvoorbeeld ‘ik’) te koppelen aan positieve karaktereigenschappen (bijvoorbeeld ‘slim’). De woorden werden subliminaal aangeboden en dit betekent dat woorden zo kort worden getoond dat het onder de waarnemingsdrempel blijft. Deelnemers waren zich dus niet bewust van de informatie die ze hadden gezien. Deze methode staat bekend als subliminale evaluatieve conditionering ofwel SEC. Het eerste experiment was een directe replicatie van een eerdere studie [78] en onderzocht of SEC impliciet zelfvertrouwen kon verhogen in de algemene studentenpopulatie. In het tweede en derde experiment werd ook onderzocht of deze manipulatie van impliciet zelfvertrouwen invloed had op hart(re)activiteit in piekerende studenten. In totaal deden 242 studenten mee aan de drie experimenten

en hebben we nauwkeurig het effect van SEC bestudeerd. Het is opmerkelijk dat we in geen van de drie experimenten in staat waren om de eerder gerapporteerde positieve effecten van SEC op zelfvertrouwen te repliceren (ondanks het gebruik van dezelfde manipulatie en procedure). Daarnaast had SEC geen effect op onbewuste stress en hart(re)activiteit. In deze studie waren we dus niet in staat om aan te tonen dat een impliciete mentale representatie (van zelfvertrouwen) invloed had op fysiologische activiteit, omdat impliciet zelfvertrouwen niet significant was verhoogd als gevolg van de manipulatie. Wel vonden we dat individuen met een laag zelfvertrouwen, in reactie op een stressor (namelijk de veronderstelling dat een presentatie gegeven moest worden voor de camera), een grotere verhoging hadden in hartactiviteit in vergelijking met individuen met een hoog zelfvertrouwen. De verhoging in hartactiviteit als gevolg van de stressor was niet verschillend wanneer er rekening werd gehouden met het niveau van impliciet zelfvertrouwen van een individu. Deze bevinding is in tegenspraak met de uitgebreide perseveratieve cognitie hypothese, maar is gebaseerd op exploratieve analyses en omvat slechts één mogelijke operationalisatie van onbewuste stress. De resultaten dienen dus met voorzichtigheid te worden geïnterpreteerd.

In *Hoofdstuk 7* worden de bevindingen van de verschillende studies samengevat en bediscussieerd. Daarnaast worden de limitaties van het proefschrift besproken en komen zowel theoretische als klinische implicaties aan bod. Ook worden mogelijke vervolgonderzoeken voorgesteld.

CONCLUSIE

In dit proefschrift is de houdbaarheid van de (uitgebreide) perseveratieve cognitie hypothese onderzocht in het dagelijks leven. Vooralsnog is er geen direct bewijs gevonden dat (onbewuste) perseveratieve cognities een negatieve invloed hebben op de gezondheid. Dit komt mogelijk doordat we niet in staat waren om perseveratieve cognities te manipuleren en hierdoor konden we niet onderzoeken of een vermindering in perseveratieve cognities zorgt voor een verbetering van de gezondheid. Er is dus behoefte aan vervolgonderzoek dat andere technieken gebruikt om (onbewuste) perseveratieve cognities te manipuleren. Als men erin slaagt om perseveratieve cognities te veranderen, dan kan vervolgens het effect hiervan op de gezondheid bestudeerd worden. Onze bevindingen laten zien dat de online piekerinterventie de perseveratieve cognities niet verminderd en zelf gerapporteerde gezondheid niet verbeterd. Bestaand onderzoek toont aan dat interventies die worden aangeboden op de mobiele telefoon gebruikt kunnen worden om mensen gedurende de dag te trainen en ook effectief kunnen zijn in het verbeteren van de psychische gezondheid.

De mobiele interventie, die is onderzocht in dit proefschrift, bleek echter ineffectief en toekomstig onderzoek kan verder uitsluiten wat werkt voor wie. Daarnaast is er geen bewijs gevonden dat SEC een positief effect heeft op onbewuste stress of fysiologische activiteit. Aangezien stress veel voorkomt, is het belangrijk meer inzicht te krijgen in hoe stress de gezondheid negatief beïnvloedt en toekomstig onderzoek kan hieraan bijdragen.

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WE MOVE / OR WE DON'T
WE CHANGE / OR WE STAY THE SAME
[James Vincent McMorrow]

Curriculum vitae

Anke Versluis was born on December 6 1988 in Gorinchem, the Netherlands. In 2007 she completed her secondary school education at Anna van Rijn College in Nieuwegein. After graduation Anke started her Bachelor in psychology at Utrecht University and earned her bachelor's degree in 2010. Next, she started the Master program clinical and health psychology at Utrecht University and graduated cum laude in 2011. From 2011 to early 2013 Anke worked as a research and teaching assistant at the University of Amsterdam. Furthermore, in 2012, she worked as a counseling psychologist at a primary health care facility. From March 2013 to July 2017 Anke was a Ph.D. candidate in the department of health, medical, and neuropsychology at Leiden University. As part of her graduate work Anke visited the psychophysiology laboratory at the University of Arizona for five months beginning October 2016. During this time she worked closely with Prof. Richard D. Lane and Prof. John J.B. Allen on research involving emotional awareness.

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