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Cognitive control and daily affect regulation in major depression and borderline personality disorder: a study protocol

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ABSTRACT

Introduction: Affective disturbances and difficulty in affect regulation are core features of major depressive disorder (MDD) as well as borderline personality disorder (BPD). Whereas depressed individuals are characterized by affective inertia, individuals with BPD are characterized by affective instability. With regard to affect regulation, both groups have been found to use more maladaptive strategies, such as rumination or suppression, compared to healthy controls. Individuals with MDD or BPD might also employ adaptive regulation strategies (e.g., reappraisal) less *effectively* than healthy controls. Surprisingly, however, there have been hardly any studies directly comparing these two disorders to disentangle shared and disorder-specific deficits in affective dynamics and affect regulation.

Furthermore, theoretical models link deficits in affect regulation to deficits cognitive control functions. Given that individuals with MDD or BPD are both characterized by impairments in cognitive control, it will be intriguing to examine whether such impairments might explain their difficulty in affect regulation. The aim of the present study is thus to investigate the link between individual differences in cognitive control and disturbances in affect dynamics and regulation in the daily life of individuals with MDD or BPD.

Methods and Analyses: We will use a smartphone application to assess negative and positive affect as well as affect regulation strategies at eight times a day for seven days. We will further employ four computerized tasks to assess two cognitive control functions, namely interference control and discarding irrelevant information from working memory. Our hypotheses will be tested using a multi-method approach. Power analyses determined a sample size of 159 (53 MDD, 53 BPD, 53 Controls) to detect medium effect sizes.

Ethics and Dissemination: Ethics approval has been obtained from the Freie Universität Berlin. Data collection started in 01/2017 and will last till the end of 2018.

Keywords: Affect regulation, cognitive control, major depression, borderline personality disorder, interference control, discarding, ambulatory assessment

Strengths and limitations of this study

- Real-time assessment of affect dynamics and affect regulation in daily life
- Assessing two prominent affective disorders (BPD and MDD) and a control group
- Linking the use and effectiveness of affect regulation strategies to individual differences in cognitive control functions (i.e. discarding of previously relevant information, interference control)

INTRODUCTION

Affective disturbances are common among most mental disorders. In search of causes for these affective disturbances, impairments in the regulation of affective states have become a major interest in clinical psychology. The most prominent and generalized impairments in affect regulation (AR) are found in individuals with major depressive disorder (MDD) or borderline personality disorder (BPD)[1 2]. Although there is growing research examining abnormalities in the use and effectiveness of AR strategies, hardly any study has directly compared these two disorders to disentangle shared and disorder-specific deficits in affect regulation. In addition, theoretical models have linked effective AR to cognitive control functions, for reviews see[3 4]. Identification of abnormalities in affect regulation and its underlying cognitive mechanisms thus represents an important step in developing interventions to address deficits in affect regulation in these disorders.

The following paragraphs give an overview of previous findings on the use and effect of the three most researched AR strategies, i.e. rumination, suppression, and reappraisal in MDD and BPD, while highlighting important questions that have as yet remained unanswered.

Affect regulation in depression

Affective disturbances in depression are characterized by both the experience of sustained negative affect i.e., affective inertia, [5], as well as difficulty experiencing positive affect. To gain a better understanding of these affective disturbances, recent research has focused on the way depressed individuals attempt to regulate their affect. Results revealed that depressed individuals as compared to healthy controls show a greater use of putatively maladaptive affect regulation strategies, for a review, see [6]. In this context, rumination has been identified as a particularly detrimental response to negative affect[2]. Rumination involves recurrent negative thoughts focused on one's depressive symptoms and the causes, meaning, and

consequences of these symptoms[7]. Rumination in response to negative affect has been shown to intensify negative affect, increase negative memory recall, impair social problem solving, and ultimately enhance the risk for the onset of new depressive episodes, for a review, see [8]. Another maladaptive regulation strategy that has been linked to depression is the suppression of one's affect. Currently depressed as well as remitted depressed individuals have been found to suppress their affective response to a greater degree than non-depressed individuals[6 9]. Although intended to reduce negative affect, suppression has been found to increase negative affect[9 10]. On the other hand, evidence also suggests that depressed individuals are less likely to use AR strategies that are beneficial in healthy individuals[11]. Cognitive reappraisal has been shown to be a particularly effective means of AR[12]. Reappraisal involves changing the meaning of a situation in order to alter the affect that follows[13]. In a recent meta-analysis, decreased habitual use of reappraisal has been associated with depressive symptoms[6]. Thus, evidence suggests that depression is associated with more frequent use of maladaptive AR strategies, such as rumination or suppression, and less frequent use of adaptive strategies, such as reappraisal.

In addition, there is evidence suggesting that depressed individuals are not able to employ putatively adaptive ER strategies as effectively as healthy individuals. Joormann and colleagues, for example, demonstrated that currently depressed compared to healthy individuals were not able to use positive memories to repair a negative affective state[14]. Further research found that higher levels of depressive symptoms were associated with lower reappraisal ability under high levels of stress[15]. Thus, strategies that are effective in regulating negative affect in healthy individuals may not be as effective in the regulation of negative affect in currently depressed individuals.

Affect regulation in borderline personality disorder

The affective disturbance that is "at the core of borderline pathology"[16] is a pronounced instability of emotions[17]. Pivotal to the understanding of this pronounced instability are abnormalities in the processing and regulation of affective responses[18 19].

Regarding affect regulation, evidence suggests a more pronounced use of affect suppression in BPD[20 21]. In addition, heightened levels of rumination have been reported in BPD as compared to healthy individuals[22 23]. Students with pronounced traits of borderline personality demonstrate a generally increased use of adaptive as well as maladaptive AR strategies to regulate affective states[24].

Only recently, studies have begun to examine the effectiveness of AR strategies in BPD. In contrast to findings in healthy individuals and patients with MDD, the suppression of affective responses was found to decrease negative affect and to attenuate impulsive behavior[25]. Recent findings provided further support that affect suppression may have an adaptive function in BPD[26]. In addition, findings suggest that individuals with BPD as compared to healthy controls use cognitive reappraisal less efficiently to attenuate negative affect[27 28]. This might be due to difficulties in the generation and implementation of alternative appraisals of affect-generating stimuli[18].

Affect regulation and cognitive control deficits

The mechanisms underlying impairments in effective affect regulation are not yet well researched. Several researchers have suggested that cognitive control functions play an important role in effective affect regulation[3 4]. Affective states are associated with the activation of affect congruent cognitions in working memory. The ability to control affective contents in working memory may thus be essential for effective affect regulation. It is important to note, that cognitive control is not a unitary construct but consists of several components, such as response inhibition, discarding of no longer relevant material from working memory, or interference control (i.e. resistance to distractor interference)[29 30].

Impairments in cognitive control have been generally linked to both BPD[31-34] and depression symptoms[35-38]. Importantly, impairments in cognitive control have also been directly linked to disturbances in affect regulation: more frequent *use* of rumination has been related to difficulty discarding no longer relevant material from working memory[39], whereas more frequent use of suppression has been linked to impairments in interference control of negative material[40]. In addition, less frequent use of reappraisal may be related to difficulty in interference control[40 41].

Fewer studies have assessed the role cognitive control plays in the *effectiveness* of ER strategies. First evidence implies that deficits in the ability to discard previously relevant information from working memory confine the benefits of reappraisal and increase the detrimental effects of rumination[42 43]. However, this has not yet been assessed in a clinical sample. It will therefore be crucial to examine the link between differences in the cognitive control of affective material and the effectiveness of daily affect regulation in clinical samples.

Research questions and hypotheses

The present project combines the assessment of daily affective dynamics, daily affect regulation strategies, and cognitive control abilities in individuals with MDD, individuals with BPD, and healthy controls. This design is a compelling framework to examine the following research questions:

1. Affective Dynamics

Research Question: Do healthy controls, individuals with MDD, and individuals with BPD differ in their affective dynamics (i.e., affective inertia, affective instability) in daily life?

Hypotheses: We expect a main effect of group on each measure of affect dynamics. Specifically, we expect that individuals with BPD show more affective instability than

individuals with MDD or healthy controls, when controlling for affective variability[5]. Further, we expect that individuals with MDD or BPD show higher affective variability than healthy controls, even after controlling for inertia. Finally, we expect that individuals with BPD show less affective inertia than individuals with MDD or healthy controls, when controlling for affective variability.

2. Use of affect regulation strategies

Research Question: Do healthy controls, individuals with MDD, and individuals with BPD differ in their habitual use of different affect regulation strategies?

Hypotheses: First, we expect a main effect of group on general intensity of affect regulation. That is, we expect that individuals with BPD or MDD generally employ affect regulation strategies more often than healthy controls. Second, we expect an interaction between group and kind of strategy [6 20 22 24]. That is, we expect that individuals with BPD or MDD select rumination or suppression more often than reappraisal. In contrast, we expect that healthy controls select reappraisal more often than rumination or suppression.

3. Effect of affect regulation strategies on affect

Research Questions: Does the effectiveness of affect regulation strategies differ between healthy controls, individuals with MDD, and individuals with BPD?

Hypotheses: We expect an interaction effect between group and kind of strategy on affect ratings. Specifically, we expect that **rumination** intensity assessed as time t will be associated with higher negative affect at time t when controlling for negative affect at t-1 in individuals with MDD or BPD than in healthy controls[44 45]. Note, that rumination assessed at time t reflects the intensity in the interval between time t-1 and time t.

The intensity of **suppression** assessed at time t will be associated with lower negative affect at time t when controlling for negative affect at t-1 in individuals with BPD[24 26], but not in individuals with MDD and healthy controls[9 10].

The intensity of **reappraisal** assessed at time t will be associated with more negative affect at time t when controlling for negative affect at t-1in individuals with BPD or MDD as compared to healthy controls[15 18 27].

4. Group differences in cognitive control

Research Question: Do healthy controls, individuals with MDD, and individuals with BPD differ in their ability to control affective material in working memory?

Hypotheses: We expect an interaction effect between group and experimental condition on response latencies. Specifically, we expect that individuals with MDD or BPD as compared to healthy controls show impairments in **interference control** of affective stimuli, reflected in slower response latencies in experimental as compared to control trials[31 46].

Similarly, we expect that individuals with MDD as compared to healthy controls show impairments in **discarding** no longer relevant negative material from working memory, reflected in slower response latencies in experimental as compared to control trials[37].

5. Cognitive control and affect regulation

Research question: Are impairments in cognitive control functions related to differences in the use or effectiveness of affect regulation strategies?

Hypotheses: We expect an interaction between the respective cognitive control index and kind of strategy on intensity ratings (i.e., strategy use). That is, we expect that individual differences in **discarding** affective material from working memory will be negatively associated with more frequent use of rumination[37 39 40].

In addition, we expect that individual differences in **interference control** will be negatively associated with using suppression and positively associated with using reappraisal[37].

We further expect an interaction between the respective cognitive control index and kind of strategy on negative affect ratings at time t. That is, we expect that individual differences in **discarding** affective material from working memory when using rumination will be associated with higher negative affect at time t when controlling for negative affect at time t-1[42 43]. Further, we expect that individual differences in discarding affective material from working memory when using reappraisal will be associated with less negative affect at time t when controlling for negative affect at time t-1[42 43].

Note, that the number of studies directly comparing individuals with MDD and BPD regarding affective dynamics, affect regulation strategies, or cognitive control abilities is very limited. Thus, the literature only allows to formulate specific hypotheses on differences between the clinical groups and the control group. It will be intriguing to examine differences and similarities between individuals with MDD and individuals with BPD in the assessed variables.

METHODS AND ANALYSES

Participants

The present research project includes three groups of participants: individuals with BPD, individuals with current MDD, and healthy control participants. The sample size is targeted at 53 participants per group (for details see power analysis).

General inclusion and exclusion criteria

Participants will be between age 18 and 65 years and speak German as their native language (due to verbal demands in the experimental tasks). Participants need to provide written informed consent for participation in the study. Participants will be excluded if they

- are pregnant,
- report of severe head trauma or any known neurological diseases,
- report any past or present psychotic symptoms,
- meet criteria for bipolar disorder or any psychotic disorder,
- meet criteria for substance dependency within the last 12 months

Patients taking psychotropic medication will not be excluded. However, there must be no change in medication for at least four weeks prior to as well as during the entire assessment period. Medication type and dose will be assessed. In-patients will not be included in the study.

Major Depressive Disorder (MDD) group

Participants included in the MDD group will meet Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for a current major depressive episode. The duration of the current episode as well as the number of past episodes will be assessed but won't be decisive for inclusion into the study. Due to high rates of comorbidity among MDD and other

mood and anxiety disorders, individuals with a comorbid mood (except bipolar disorders) or anxiety disorder will be included. Depressed individuals meeting more than two DSM-IV criteria for BPD will be excluded.

Borderline personality disorder (BPD) group

Participants included in the BPD group will meet DSM-IV criteria for borderline personality disorder. Due to high rates of Axis-I and Axis-II comorbidity in BPD presence of comorbid disorders will be allowed for study inclusion with the exception of a current major depressive episode, substance dependency within the last 12 months, bipolar or psychotic disorders.

Healthy control group

Participants included in the healthy control group have to be free of any past or present mental disorder according to DSM-IV criteria. The absence of any mental disorder will be confirmed by Structured Clinical Interview for DSM (SCID-I) and SCID-II interviews. Participants in the control group will be free of any psychotropic medication. Furthermore, control participants will be excluded if they meet more than two DSM-IV criteria for BPD or any of the two cardinal DSM-IV criteria for MDD.

Recruitment

Individuals with MDD or BPD will be recruited through advertisements posted at cooperating counseling institutions, various sites within the community, and in online newspapers. Healthy control participants will be recruited through postings at various sites within the community and in online newspapers.

In addition, depressed participants will be recruited from the local outpatient clinic at Freie Universität Berlin (Head: Prof. Dr. Babette Renneberg). Participants with BPD will also

be recruited at the Department for Psychiatry and Psychotherapy at Charité Berlin (Head: Prof. Dr. Stefan Röpke).

Assessment of psychopathology

All participants will be interviewed using the Structured Clinical Interview for DSM-IV Axis-I[47] and Axis-II disorders[48]. Diagnostic interviews will be conducted by trained interviewers. Participants' intelligence will be estimated by measuring cognitive capabilities[49].

The following instruments will assess disorder-specific and general psychopathology: The Beck Depression Inventory II (BDI-II)[50 51]; the Borderline Symptom List (BSL-23)[52]; the Brief Symptom Inventory (BSI)[53 54]; the German version of the 10-item Response Style Questionnaire (RSQ)[55]. Finally the German version of the Positive and Negative Affect Schedule (PANAS)[56] as well as the Dissociative Tension Scale (DSS-4)[57] will be used to assess mood fluctuations and dissociative states in the laboratory sessions.

In addition, all individuals with BPD or MDD will be asked about any current and/or past psychotherapy.

Ambulatory assessment of daily affect and affect regulation

All participants receive a smartphone including an App for ambulatory assessment. Participants will be instructed to go on with their daily activities and respond to several questions when indicated by a beep. The Smartphone App will be individually programmed to beep 8 times a day for 7 consecutive days with the daily sampling period comprising 12 hours. The sampling period will be divided into 8 time blocks of equal length and the auditory signal will occur pseudo-randomly within each time block, with a minimum of 1h between beeps[42]. Responses will be time-stamped by the software.

Following each prompt, participants will indicate on a scale from 1 (not at all) to 7 (very much) how angry, anxious, ashamed, cheerful, depressed, happy, and tense they feel

(i.e. 'How did you feel just before the beep?'). Given that individuals with BPD may have problems in correct emotion identification, the average score across all negative affect ratings (i.e., angry, anxious, ashamed, depressed, tense) will be used to assess the impact of ER strategies on negative affect. Next, participants will be asked to indicate on a scale from 1 (not at all) to 7 (very much) how much they used the following strategies since the last beep: rumination ('I thought over and over again about a situation or my feelings'; 'How negative were these thoughts?'), suppression ('I controlled my emotion by not showing them'), reappraisal (I have thought about the situation in a different way.'). To control for overall degree of ER strategy use[24], participants are also asked about the implementation of other widely used or disorder-relevant ER strategies[16 58]. These are acceptance ('I accepted the situation and/or my situation'), distraction ('I found an activity to keep myself busy and distracted'), and social sharing ('I found someone to talk to about my feelings'). In addition, individuals with a history of self-injurious behavior will be asked how much they felt an urge to injure themselves. At the first daily beep, all participants will be asked to indicate on a scale from 1 (not at all) to 7 (very well) how well they slept last night.

Participants will receive an extra incentive for responding to more than 90% of beeps.

Assessment of cognitive control

1. Discarding of no longer relevant information from working memory

Working Memory Selection Task (WMST)

The WMST assesses the ability to discard no longer relevant affective information from working memory[37].

Each trial of the WMST consists of three consecutive displays: a learning display, a cue display, and a probe display. On the learning display, participants are presented with two rows of three words each, one row printed in red and the other row printed in blue.

Participants are instructed to memorize all six words. On the following cue display, a red or blue frame is presented indicating which row of words will be relevant for the upcoming response. Participants are instructed to keep only the relevant set in mind and disregard the other three words. Finally, on the probe display, a probe word is presented and participants are asked to decide whether or not the probe is from the relevant word set.

The probe may either be a word from the relevant word set (relevant probe), a word that participants had to learn but were then asked to forget (suppress probe), or a new word that had not been presented before (novel probe). Thus, participants have to reject both suppress probes and novel probes. It has been shown that participants take longer to reject a suppress probe compared to a novel probe[59] and it has been suggested that this difference in reaction times reflects the residual activation of the no-longer-relevant suppress word. Thus, the ability to discard no longer relevant material from working memory is measured by reaction times (RT) to suppress probes compared to novel probes. In the present version of the task, on critical trials, the red and blue rows of words include either only positive or only negative words, and the two rows always differ in valence. Thus, here we will compare the ability to discard irrelevant negative or positive information, respectively. All word stimuli are taken from the Berlin Affective Word List Reloaded (BAWL-R)[60].

Removal and Updating Task (RUT)

The Removal and Updating Task is based on a letter updating task[61] adapted by Chang, Ecker & Page[62]. It measures the ability to remove no longer relevant affective contents from working memory (WM).

Each trial begins with the presentation of three words in three frames for 3000 ms and participant are asked to memorize the words. Next, the words disappear and a variable number of updating steps follows. At each updating step, one of the three words is cued for removal, indicated by the respective frame turning into red color. Then, a new word is

presented in the cued frame and participants are asked to replace in mind the memorized word with the new word. Participants indicate the completion of their updating process by key-press. The reaction time between the presentation of the new word and participants' key-press serves as dependent variable.

Importantly, the time between the removal cue and the presentation of the new word is varied ("cue-target-interval", CTI). In long CTI conditions (1500ms), the CTI allows for a complete removal process, so that the reaction time between the presentation of the new word and participants' key press only reflects the encoding of the new word. In the short CTI condition (200ms), the CTI does not allow for a complete removal process, so that the reaction time reflects the removal process and the encoding of the new word. Thus, the measure of an individual's removal speed is the comparison between RTs in trials with short and long CTI. Indices reflecting the removal of negative or positive words can be computed. All word stimuli are taken from the BAWL-R.

To control for general updating ability, participants also complete a neutral version of the removal and updating task[61] including letters instead of words.

2. Interference Control

Delayed working memory paradigm

This paradigm measures the ability to control interference from affectively distracting stimuli during working memory performance[63].

On each trial, six capital letters are presented for 1500ms and participants are asked to memorize them. The presentation of the letters is followed by a delay period of 2000 ms, and the presentation of another single letter. Participants have to decide whether or not the single letter was part of the initial block of letters. During the delay period, participants are either presented with a blank screen, a neutral or a negative picture. All picture stimuli are taken

from the International Affective Picture System (IAPS)[64]. Neutral and negative IAPS stimuli are matched for social content and perceptual complexity.

The ability to control interference from irrelevant information will be examined by comparing response latencies between blank screens, neutral, and negative stimuli presented in the delay period.

Stroop Paradigm

The Stroop task is based on a paradigm by Etkin and colleagues[65 66] and measures the ability to control interference from simultaneously presented irrelevant information.

Each trial consists of the presentation of a happy or an angry facial expression with the word "Anger" or "Happiness" printed across the facial expression. Participants are asked to ignore the words and to indicate by button press whether the face picture displays an angry or happy facial expression. Facial expressions and words are either congruent or incongruent. Each picture/word combination is presented for 1000 ms. All facial expressions are taken from the original Ekman faces set[67].

The ability to control interference from irrelevant information is assessed by the classical behavioral interference effect (i.e. response latencies to incongruent trials as compared to response latencies to congruent trials). In addition, trials can be classified based on the congruence of the previous trial: congruent trial following a congruent trial (cC), incongruent trial following a congruent trail (cI), congruent trial following an incongruent trial (iC), and incongruent trial following an incongruent trial (iI).

Additional Measures

Prediction and Recall of affect, sleep, and affect regulation strategies

In the first laboratory session, participants will be presented with all items from the ambulatory assessment (e.g., affect, affect regulation strategies, sleep) and asked to indicate

on a scale from 0 (not at all) to 7 (very much) how much they expect to feel or behave this way (on average) during the following seven days. At the end of the ambulatory assessment period, participants will be presented with all items from the ambulatory assessment again and asked to indicate on a scale from 0 (not at all) to 7 (very much) how much they had felt or behaved this way (on average) during the past seven days.

Electrocardiogram

At the end of the second laboratory session, participants will be asked to put on an ECG chest belt to measure their resting state heart rate variability for a 5-minute period. Participants are asked to relax during the ECG assessment.

Movement

During the seven-day ambulatory assessment period, participants will be asked to wear an accelerometer attached to their hips. The accelerometer continuously assesses data regarding participants' acceleration in all three geometric axes, context temperature, and air pressure[68]. This will allow to examine individual levels of physical activity and energy expenditure during the ambulatory assessment period.

Procedures

The procedure of this project is depicted in Figure 1. Ethics approval has been obtained from the Freie Universität Berlin. Data collection started in 01/2017 and will last till the end of 2018.

Sample size determination

Power analysis for group differences in cognitive control

Previous studies examining impairments in valence-dependent cognitive control in depressed compared to control participants yielded medium between group effect sizes (WMST task: e.g., d=0.78)[37]. Similar effect sizes were obtained for group differences in valence-dependent cognitive control between individuals with BPD and healthy controls (interference control: e.g., d=0.89)[31]. To detect medium sized group differences in cognitive control functions using univariate ANOVAs, a total sample size of N=159 (N=53 per group) is needed as determined using G*Power (assuming α=.05, power of .8). For selected post-hoc group comparisons, a group size of N=51 is required (assuming α=.05, power of .8, allocation ratio = 1). Note, that we will use multi-level modeling to test group differences in cognitive control. Given that multi-level modeling includes several assessment points per individual, the intended sample size of N=159 will be more than sufficient to detect medium sized group differences in cognitive control using multi-level modeling.

Power analysis for ambulatory assessment data

A sample size of N=159 that is required for the experimental part of the study is also large enough to ensure appropriate power for analyzing the ambulatory assessment data. For the ambulatory assessment part, all variables will be assessed 8 times a day for 7 consecutive days. For the multilevel analysis this would mean that there are 56 occasions of measurement nested within 159 individuals resulting in 8904 data points. For variable affective states it is reasonable to assume an intraclass correlation of 0.30 resulting in a design effect of DE = 21.7[69]. Therefore, our multilevel analysis would be approximately comparable to a classical multiple regression analysis with 410 individuals[69]. Given this sample size it would be possible to detect a small interaction effect between two independent variables (partial R2 = 0.01) in a multiple regression analysis with a power of .8 (assuming α=.05).

Data analysis

1. Affective dynamics

To assess whether groups differ in their affective dynamics (i.e., inertia, instability, variability), we will calculate three different within-person measures for both positive and negative affect[70]: (a) Affective variability will be assessed by the within-subject standard deviation of the respective affect scale. (b) Affective instability will be calculated as the within-subject root Mean Square Successive Difference (rMSSD) between consecutive affect measures. (c) Inertia will be assessed by the temporal dependency of consecutive affect measures, i.e., the within-subject lag-one autocorrelation. Autocorrelations will be Fisher's z transformed to normalize their distribution.

Based on the distribution of the respective indices, we will select adequate methods for testing group differences. We will further examine whether controlling for mean levels of positive or negative affect will have an impact on the main effect of Group[71].

2./3. Group differences in the use and effectiveness of affect regulation strategies

To examine whether groups differ in the frequency of using rumination, suppression, or reappraisal, we will employ hierarchical linear modeling. The dependent variable will be the intensity rating of the ER strategies assessed at time t. The predictor variables of interest will be Group (BPD, MDD, CTL) and the specific Strategy (reappraisal, rumination, suppression, distraction, acceptance, social sharing).

To examine whether the effectiveness of rumination, suppression, or reappraisal differs among groups, we will employ hierarchical linear modeling. The dependent variable will be the respective affect rating (positive or negative) at time t. Affect ratings at time t-1 will be entered as predictor. Predictor variables of main interest will be Group (BPD, MDD, CTL) and the intensity of each assessed ER Strategy (reappraisal, rumination, suppression, distraction, acceptance, social sharing) employed between time t-1 and time t.

4. Group differences in cognitive control functions

Reaction time data from the behavioral experiments will be cleansed according to the following procedures: outliers in response latencies will be defined as values below or above the upper or lower fences of each individual's distribution in each experimental condition. Outliers will be eliminated. In addition, participants will be excluded from analyses if their overall accuracy level indicates that the task was not sufficiently understood.

In a first step, group differences in cognitive control functions will be analyzed using separate multi-level models per experiment. Response latency will be the dependent variable. The Experimental Condition, Stimuli Valence (where applicable), and Group will be entered as predictor variables.

In a second step, composite scores for the ability to discard irrelevant information from working memory, and for the ability to control interference from distracting information will be generated. Group differences on these composite scores will be examined by using multi-level models. The respective composite score will be the dependent variable. Stimuli Valence and Group will be entered as predictor variables.

5. Relating cognitive control functions and affect regulation

a. To examine whether the *use* of rumination, suppression, or reappraisal will be related to individual differences in cognitive control functions, we will employ hierarchical linear modeling. The dependent variable will be the intensity rating of the ER strategies assessed at time t. The predictor variables of interest will be the specific Strategy (reappraisal, rumination, suppression, distraction, acceptance, social sharing), and the Cognitive Control scores, as detailed below.

b. To examine whether the *effectiveness* of reappraisal, rumination, or suppression will be related to individual differences in cognitive control functions, we will also employ hierarchical linear modeling. The dependent variable will be the respective affect rating

(positive or negative) at time t. Affect ratings at time t-1 will be entered as predictor variable (see 2./3.). Further predictor variables of interest will be Group (BPD, MDD, CTL), the Cognitive Control scores (see below), and the Intensity of each assessed ER strategy (reappraisal, rumination, suppression, distraction, acceptance, social sharing) employed between time t-1 and time t.

Cognitive control indices for each experiment will be computed as follows: For the 'Working Memory Selection Task', the discarding index will be computed as the median response latency to suppress probes minus the median response latency to novel probes of the same valence. Two separate difference scores, one for each valence condition (positive, negative), will be computed.

For the Removal and Updating task, the removal index will be assessed as the difference in response latencies between trials with short and long CTIs. This difference will be computed as a proportional gain score accounting for general processing speed (i.e., Removal Speed = [mean(short CTI) – mean(long CTI)] / mean(short CTI)). We will calculate two separate removal time indices for the removal of negative and positive words, respectively.

For the Stroop Task, the classical behavioral interference effect (i.e. response latencies to incongruent trials minus response latencies to congruent trials) will be computed.

In the ‘Delayed Working Memory Task', a general distraction score will be computed by subtracting response latencies in trials with blank screens presented in the delay period from response latencies in trials with neutral and negative IAPS stimuli presented in the delay period. In addition, we will calculate an ‘affective distraction score’ by subtracting response latencies for neutral stimuli from response latencies for negative stimuli.

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Figures

Figure 1. Procedure of the research project

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Conflict of Interests

All authors declare that there are no conflicts of interest.

Contributorship Statement

Lars Schulze and Ulrike Zetsche designed the study, wrote the funding grant, and drafted and revised the current manuscript. Paul Christian Bürkner was responsible for the data analytic plan, wrote the section data analysis, and revised the current manuscript. Julian Bohländer piloted the Removal and Updating task, coordinates the data assessment, and wrote and revised the current manuscript.

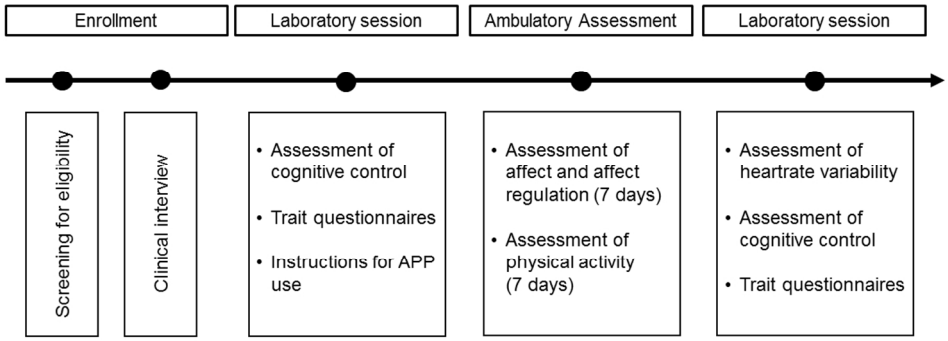

Figure 1. Procedure of the research project

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Cognitive control and daily affect regulation in major depression and borderline personality disorder: protocol for an experimental ambulatory assessment study in Berlin, Germany

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ABSTRACT

Introduction: Affective disturbances and difficulty in affect regulation are core features of major depressive disorder (MDD) as well as borderline personality disorder (BPD). Whereas depressed individuals are characterized by affective inertia, individuals with BPD are characterized by affective instability. With regard to affect regulation, both groups have been found to use more maladaptive strategies, such as rumination or suppression, compared to healthy controls. Individuals with MDD or BPD might also employ adaptive regulation strategies (e.g., reappraisal) less *effectively* than healthy controls. Surprisingly, however, there have been hardly any studies directly comparing these two disorders to disentangle shared and disorder-specific deficits in affective dynamics and affect regulation.

Furthermore, theoretical models link deficits in affect regulation to deficits cognitive control functions. Given that individuals with MDD or BPD are both characterized by impairments in cognitive control, it will be intriguing to examine whether such impairments might explain their difficulty in affect regulation. The aim of the present study is thus to investigate the link between individual differences in cognitive control and disturbances in affect dynamics and regulation in the daily life of individuals with MDD or BPD.

Methods and Analyses: We will use a smartphone application to assess negative and positive affect as well as affect regulation strategies at eight times a day for seven days. We will further employ four computerized tasks to assess two cognitive control functions, namely interference control and discarding irrelevant information from working memory. Our hypotheses will be tested using a multi-method approach. Power analyses determined a sample size of 159 (53 MDD, 53 BPD, 53 Controls) to detect medium effect sizes.

Ethics and Dissemination: Ethics approval has been obtained from the Freie Universität Berlin. Data collection started in 01/2017 and will last till the end of 2018.

Keywords: Affect regulation, cognitive control, major depression, borderline personality disorder, interference control, discarding, ambulatory assessment

Strengths and limitations of this study

- Real-time assessment of affect dynamics and affect regulation in daily life
- Assessing two prominent affective disorders (BPD and MDD) and a control group
- Linking the use and effectiveness of affect regulation strategies to individual differences in cognitive control functions (i.e. discarding of previously relevant information, interference control)
- Limitations: Cross-sectional design, mainly self-report measures of affect regulation

INTRODUCTION

Affective disturbances are common among most mental disorders. In search of causes for these affective disturbances, impairments in the regulation of affective states have become a major interest in clinical psychology. The most prominent and generalized impairments in affect regulation (AR) are found in individuals with major depressive disorder (MDD) or borderline personality disorder (BPD)[1 2]. Although there is growing research examining abnormalities in the use and effectiveness of AR strategies, hardly any study has directly compared these two disorders to disentangle shared and disorder-specific deficits in affect regulation. In addition, theoretical models have linked effective AR to cognitive control functions, for reviews see [3 4]. Identification of abnormalities in affect regulation and its underlying cognitive mechanisms thus represents an important step in developing interventions to address deficits in affect regulation in these disorders.

The following paragraphs give an overview of previous findings on the use and effect of the three most researched AR strategies, i.e. rumination, suppression, and reappraisal in MDD and BPD, while highlighting important questions that have as yet remained unanswered.

Affect regulation in depression

Affective disturbances in depression are characterized by both the experience of sustained negative affect (i.e., affective inertia, [5]) as well as difficulty experiencing positive affect [6]. To gain a better understanding of these affective disturbances, recent research has focused on the way depressed individuals attempt to regulate their affect. Results revealed that depressed individuals as compared to healthy controls show a greater use of putatively maladaptive affect regulation strategies, for a review, see [7]. In this context, rumination has been identified as a particularly detrimental response to negative affect [2]. Rumination involves recurrent negative thoughts focused on one's depressive symptoms and the causes, meaning, and

consequences of these symptoms [8]. Rumination in response to negative affect has been shown to intensify negative affect, increase negative memory recall, impair social problem solving, and ultimately enhance the risk for the onset of new depressive episodes, for a review, see [9]. Another maladaptive regulation strategy that has been linked to depression is the suppression of one's affect. Currently depressed as well as remitted depressed individuals have been found to suppress their affective response to a greater degree than non-depressed individuals [7 10]. Although intended to reduce negative affect, suppression has been found to increase negative affect [10 11]. On the other hand, evidence also suggests that depressed individuals are less likely to use AR strategies that are beneficial in healthy individuals [12]. Cognitive reappraisal has been shown to be a particularly effective means of AR [13]. Reappraisal involves changing the meaning of a situation in order to alter the affect that follows [14]. In a recent meta-analysis, decreased habitual use of reappraisal has been associated with depressive symptoms [7]. Thus, evidence suggests that depression is associated with more frequent use of maladaptive AR strategies, such as rumination or suppression, and less frequent use of adaptive strategies, such as reappraisal. Please note that all hypotheses of the present project focus on these three most-researched AR strategies (i.e., rumination, suppression, reappraisal). When examining group differences in the use of specific AR strategies, however, it is important to control for overall AR strategy use [15]. For this purpose, we also assess other widely used strategies, namely distraction, acceptance, and social sharing. Whereas findings on the association between distraction and depression are inconclusive [2], there are hardly any studies on the association of acceptance or social sharing and depression. Thus, we do not formulate any specific hypotheses regarding these AR strategies.

In addition, there is evidence suggesting that depressed individuals are not able to employ putatively adaptive AR strategies as effectively as healthy individuals. Joormann and colleagues, for example, demonstrated that currently depressed compared to healthy individuals were not able to use positive memories to repair a negative affective state [16].

Further research found that higher levels of depressive symptoms were associated with lower reappraisal ability under high levels of stress [17]. Thus, strategies that are effective in regulating negative affect in healthy individuals may not be as effective in the regulation of negative affect in currently depressed individuals.

Affect regulation in borderline personality disorder

The affective disturbance that is "at the core of borderline pathology" [18] is a pronounced instability of emotions [19]. Pivotal to the understanding of this pronounced instability are abnormalities in the processing and regulation of affective responses [20 21].

Regarding affect regulation, evidence suggests a more pronounced use of affect suppression in BPD [22 23]. In addition, heightened levels of rumination have been reported in BPD as compared to healthy individuals [24 25]. Students with pronounced traits of borderline personality demonstrate a generally increased use of adaptive as well as maladaptive AR strategies to regulate affective states [26].

Only recently, studies have begun to examine the effectiveness of AR strategies in BPD. In contrast to findings in healthy individuals and patients with MDD, the suppression of affective responses was found to decrease negative affect and to attenuate impulsive behavior [27]. Recent findings provided further support that affect suppression may have an adaptive function in BPD [28]. In addition, findings suggest that individuals with BPD as compared to healthy controls use cognitive reappraisal less efficiently to attenuate negative affect [29 30]. This might be due to difficulties in the generation and implementation of alternative appraisals of affect-generating stimuli [20].

Affect regulation and cognitive control deficits

The mechanisms underlying impairments in effective affect regulation are not yet well researched. Several researchers have suggested that cognitive control functions play an

important role in effective affect regulation [3 4]. Affective states are associated with the activation of affect congruent cognitions in working memory. The ability to control affective contents in working memory may thus be essential for effective affect regulation. It is important to note, that cognitive control is not a unitary construct but consists of several components, such as response inhibition, discarding of no longer relevant material from working memory, or interference control (i.e. resistance to distractor interference) [31 32].

Impairments in cognitive control have been generally linked to both BPD [33-36] and depression symptoms [37-40]. Importantly, impairments in cognitive control have also been directly linked to disturbances in affect regulation: more frequent *use* of rumination has been related to difficulty discarding no longer relevant material from working memory [41], whereas more frequent use of suppression has been linked to impairments in interference control of negative material [42]. In addition, less frequent use of reappraisal may be related to difficulty in interference control [42 43].

Fewer studies have assessed the role cognitive control plays in the *effectiveness* of AR strategies. First evidence implies that deficits in the ability to discard previously relevant information from working memory confine the benefits of reappraisal and increase the detrimental effects of rumination [15 44]. However, this has not yet been assessed in a clinical sample. It will therefore be crucial to examine the link between differences in the cognitive control of affective material and the effectiveness of daily affect regulation in clinical samples.

Research questions and hypotheses

The present project combines the assessment of daily affective dynamics, daily affect regulation strategies, and cognitive control abilities in individuals with MDD, individuals with BPD, and healthy controls. This design is a compelling framework to examine the following research questions:

1. Affective Dynamics

Research Question: Do healthy controls, individuals with MDD, and individuals with BPD differ in their affective dynamics (i.e., affective inertia, affective instability) in daily life?

Hypotheses: We expect a main effect of group on each measure of affect dynamics. Specifically, we expect that individuals with BPD show more affective instability than individuals with MDD or healthy controls, when controlling for affective variability [5]. Further, we expect that individuals with MDD or BPD show higher affective variability than healthy controls, even after controlling for inertia. Finally, we expect that individuals with BPD show less affective inertia than individuals with MDD or healthy controls, when controlling for affective variability.

2. Use of affect regulation strategies

Research Question: Do healthy controls, individuals with MDD, and individuals with BPD differ in their habitual use of different affect regulation strategies?

Hypotheses: First, we expect a main effect of group on general intensity of affect regulation. That is, we expect that individuals with BPD or MDD generally employ affect regulation strategies more often than healthy controls. Second, we expect an interaction between group and kind of strategy [7 22 24 26]. That is, we expect that individuals with BPD or MDD select rumination or suppression more often than reappraisal. In contrast, we expect that healthy controls select reappraisal more often than rumination or suppression.

3. Effect of affect regulation strategies on affect

Research Questions: Does the effectiveness of affect regulation strategies differ between healthy controls, individuals with MDD, and individuals with BPD?

Hypotheses: We expect an interaction effect between group and kind of strategy on affect ratings. Specifically, we expect that **rumination** intensity assessed as time t will be associated with higher negative affect at time t when controlling for negative affect at t-1 in individuals with MDD or BPD than in healthy controls [45 46]. Note, that rumination assessed at time t reflects the intensity in the interval between time t-1 and time t.

The intensity of **suppression** assessed at time t will be associated with lower negative affect at time t when controlling for negative affect at t-1 in individuals with BPD [26 28], but not in individuals with MDD and healthy controls [10 11].

The intensity of **reappraisal** assessed at time t will be associated with more negative affect at time t when controlling for negative affect at t-1in individuals with BPD or MDD as compared to healthy controls [17 20 29].

4. Group differences in cognitive control

Research Question: Do healthy controls, individuals with MDD, and individuals with BPD differ in their ability to control affective material in working memory?

Hypotheses: We expect an interaction effect between group and experimental condition on response latencies. Specifically, we expect that individuals with MDD or BPD as compared to healthy controls show impairments in **interference control** of affective stimuli, reflected in slower response latencies in experimental as compared to control trials [34 47].

Similarly, we expect that individuals with MDD as compared to healthy controls show impairments in **discarding** no longer relevant negative material from working memory, reflected in slower response latencies in experimental as compared to control trials [38].

5. Cognitive control and affect regulation

Research question: Are impairments in cognitive control functions related to differences in the use or effectiveness of affect regulation strategies?

Hypotheses: We expect an interaction between the respective cognitive control index and kind of strategy on intensity ratings (i.e., strategy use). That is, we expect that individual differences in **discarding** affective material from working memory will be negatively associated with more frequent use of rumination [38 41 42].

In addition, we expect that individual differences in **interference control** will be negatively associated with using suppression and positively associated with using reappraisal [38].

We further expect an interaction between the respective cognitive control index and kind of strategy on negative affect ratings at time t. That is, we expect that individual differences in **discarding** affective material from working memory when using rumination will be associated with higher negative affect at time t when controlling for negative affect at time t-1 [15 44]. Further, we expect that individual differences in discarding affective material from working memory when using reappraisal will be associated with less negative affect at time t when controlling for negative affect at time t-1 [15 44].

Note, that the number of studies directly comparing individuals with MDD and BPD regarding affective dynamics, affect regulation strategies, or cognitive control abilities is very limited. Thus, the literature only allows to formulate specific hypotheses on differences between the clinical groups and the control group. It will be intriguing to examine differences and similarities between individuals with MDD and individuals with BPD in the assessed variables.

6. Additional research questions

The present research project allows to investigate several additional research questions that will be presented below:

Heart rate variability and affect regulation: Thayer and Lane [48] proposed that heart rate variability reflects a psychophysiological index of affect regulation capacity. Indeed several studies illustrated that individuals with low resting vagally-mediated heart rate variability (vmHRV) have difficulties with affect regulation [49 50]. Accordingly, lower HRV has been reported for individuals with BPD and MDD [51 52], but to date no study directly assessed the role of vmHRV on affective dynamcis or affect regulation. In this study, we include a resting-state assessment of HRV to examine this question.

Physical activity: There is considerable evidence that people feel better after being physically active [53]. However, these findings are almost entirely based on interventional, between-person designs. Hence, it is unclear whether these findings translate into daily life. It will thus be interesting to examine the associations between daily physical activity and daily affective states [54]. For these reasons, participants of our study are asked to wear an accelerometer during the ambulatory assessment phase.

Expectation and recall biases of affective states: Depressive symptoms are associated with pronounced biases in the expectation and recall of affective states [55]. Notably, such biases also affect the choice and implementation of emotion regulation strategies [56 57]. These processes, however, have been primarily investigated in non-clinical samples. In this study, depressed individuals and individuals with BPD are asked to predict their average affect, sleep, and affect regulation before the ambulatory assessment phase. After the ambulatory assessment phase, they have to recall their average weekly affect, sleep, and affect regulation."

METHODS AND ANALYSES

Participants

The present research project includes three groups of participants: individuals with BPD, individuals with current MDD, and healthy control participants. The sample size is targeted at 53 participants per group (for details see power analysis).

General inclusion and exclusion criteria

Participants will be between age 18 and 65 years and speak German as their native language (due to verbal demands in the experimental tasks). Participants need to provide written informed consent for participation in the study. Participants will be excluded if they

- are pregnant,
- report of severe head trauma or any known neurological diseases,
- report any past or present psychotic symptoms,
- meet criteria for bipolar disorder or any psychotic disorder,
- meet criteria for substance dependency within the last 12 months

Patients taking psychotropic medication will not be excluded. However, there must be no change in medication for at least four weeks prior to as well as during the entire assessment period. Medication type and dose will be assessed. In-patients will not be included in the study.

Major Depressive Disorder (MDD) group

Participants included in the MDD group will meet Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for a current major depressive episode. The duration of the current episode as well as the number of past episodes will be assessed but won't be decisive for inclusion into the study. Due to high rates of comorbidity among MDD and other

mood and anxiety disorders, individuals with a comorbid mood (except bipolar disorders) or anxiety disorder will be included. Depressed individuals meeting more than two DSM-IV criteria for BPD will be excluded.

Borderline personality disorder (BPD) group

Participants included in the BPD group will meet DSM-IV criteria for borderline personality disorder. Due to high rates of Axis-I and Axis-II comorbidity in BPD presence of comorbid disorders will be allowed for study inclusion with the exception of a current major depressive episode, substance dependency within the last 12 months, bipolar or psychotic disorders. To control for the influence of total symptom severity, all analyses on group differences in affect regulation or cognitive control will be repeated including the Brief Symptom Inventory (BSI) total score as a covariate.

Healthy control group

Participants included in the healthy control group have to be free of any past or present mental disorder according to DSM-IV criteria. The absence of any mental disorder will be confirmed by Structured Clinical Interview for DSM (SCID-I) and SCID-II interviews. Participants in the control group will be free of any psychotropic medication. Furthermore, control participants will be excluded if they meet more than two DSM-IV criteria for BPD or any of the two cardinal DSM-IV criteria for MDD.

Recruitment

Individuals with MDD or BPD will be recruited through advertisements posted at cooperating counseling institutions, various sites within the community, and in online newspapers. Healthy control participants will be recruited through postings at various sites within the community and in online newspapers.

In addition, depressed participants will be recruited from the local outpatient clinic at Freie Universität Berlin (Head: Prof. Dr. Babette Renneberg). Participants with BPD will also be recruited at the Department for Psychiatry and Psychotherapy at Charité Berlin (Head: Prof. Dr. Stefan Röpke).

Assessment of psychopathology

All participants will be interviewed using the Structured Clinical Interview for DSM-IV Axis-I [58] and Axis-II disorders [59]. Diagnostic interviews will be conducted by trained interviewers.

The following instruments will assess disorder-specific and general psychopathology: The Beck Depression Inventory II (BDI-II) [60 61]; the Borderline Symptom List (BSL-23) [62]; the Brief Symptom Inventory (BSI) [63 64]; the German version of the 10-item Response Style Questionnaire (RSQ) [65]. Finally the German version of the Positive and Negative Affect Schedule (PANAS) [66] as well as the Dissociative Tension Scale (DSS-4) [67] will be used to assess mood fluctuations and dissociative states in the laboratory sessions.

In addition, all individuals with BPD or MDD will be asked about any current and/or past psychotherapy.

Ambulatory assessment of daily affect and affect regulation

All participants receive a smartphone including an App for ambulatory assessment. Participants will be instructed to go on with their daily activities and respond to several questions when indicated by a beep. The Smartphone App will be individually programmed to beep 8 times a day for 7 consecutive days with the daily sampling period comprising 12 hours. The sampling period will be divided into 8 time blocks of equal length and the auditory signal will occur pseudo-randomly within each time block, with a minimum of 1h between beeps [15]. Responses will be time-stamped by the software.

Following each prompt, participants will indicate on a scale from 1 (not at all) to 7 (very much) how angry, anxious, ashamed, cheerful, depressed, happy, and tense they feel (i.e. 'How did you feel just before the beep?'). *To examine whether groups differ in the frequency* may have problems in correctly identifying specific negative emotions, only the average score across all negative affect ratings (i.e., angry, anxious, ashamed, depressed, tense) will be used. Next, participants will be asked to indicate on a scale from 1 (not at all) to 7 (very much) how much they used the following strategies since the last beep: rumination ('I thought over and over again about a situation or my feelings'; 'How negative were these thoughts?'), suppression ('I controlled my emotion by not showing them'), reappraisal (I have thought about the situation in a different way.'). To control for overall degree of AR strategy use [26], participants are also asked about the implementation of other widely used or disorder-relevant AR strategies [18 68]. These are acceptance ('I accepted the situation and/or my situation'), distraction ('I found an activity to keep myself busy and distracted'), and social sharing ('I found someone to talk to about my feelings'). In addition, individuals with a history of self-injurious behavior will be asked how much they felt an urge to injure themselves. At the first daily beep, all participants will be asked to indicate on a scale from 1 (not at all) to 7 (very well) how well they slept last night.

Participants will receive an extra incentive for responding to more than 90% of beeps.

Assessment of cognitive control

1. Discarding of no longer relevant information from working memory

Working Memory Selection Task (WMST)

The WMST assesses the ability to discard no longer relevant affective information from working memory [38].

Each trial of the WMST consists of three consecutive displays: a learning display, a cue display, and a probe display. On the learning display, participants are presented with two rows of three words each, one row printed in red and the other row printed in blue. Participants are instructed to memorize all six words. On the following cue display, a red or blue frame is presented indicating which row of words will be relevant for the upcoming response. Participants are instructed to keep only the relevant set in mind and disregard the other three words. Finally, on the probe display, a probe word is presented and participants are asked to decide whether or not the probe is from the relevant word set.

The probe may either be a word from the relevant word set (relevant probe), a word that participants had to learn but were then asked to forget (suppress probe), or a new word that had not been presented before (novel probe). Thus, participants have to reject both suppress probes and novel probes. It has been shown that participants take longer to reject a suppress probe compared to a novel probe [69] and it has been suggested that this difference in reaction times reflects the residual activation of the no-longer-relevant suppress word. Thus, the ability to discard no longer relevant material from working memory is measured by reaction times (RT) to suppress probes compared to novel probes. In the present version of the task, on critical trials, the red and blue rows of words include either only positive or only negative words, and the two rows always differ in valence. Thus, here we will compare the ability to discard irrelevant negative or positive information, respectively. All word stimuli are taken from the Berlin Affective Word List Reloaded (BAWL-R) [70].

Removal and Updating Task (RUT)

The Removal and Updating Task is based on a letter updating task [71] adapted by Chang, Ecker & Page [72]. It measures the ability to remove no longer relevant affective contents from working memory (WM).

Each trial begins with the presentation of three words in three frames for 3000 ms and participant are asked to memorize the words. Next, the words disappear and a variable number of updating steps follows. At each updating step, one of the three words is cued for removal, indicated by the respective frame turning into red color. Then, a new word is presented in the cued frame and participants are asked to replace in mind the memorized word with the new word. Participants indicate the completion of their updating process by key-press. The reaction time between the presentation of the new word and participants' key-press serves as dependent variable.

Importantly, the time between the removal cue and the presentation of the new word is varied ("cue-target-interval", CTI). In long CTI conditions (1500ms), the CTI allows for a complete removal process, so that the reaction time between the presentation of the new word and participants' key press only reflects the encoding of the new word. In the short CTI condition (200ms), the CTI does not allow for a complete removal process, so that the reaction time reflects the removal process and the encoding of the new word. Thus, the measure of an individual's removal speed is the comparison between RTs in trials with short and long CTI. Indices reflecting the removal of negative or positive words can be computed. All word stimuli are taken from the BAWL-R.

To control for general updating ability, participants also complete a neutral version of the removal and updating task [71] including letters instead of words.

2. Interference Control

Delayed working memory paradigm

This paradigm measures the ability to control interference from affectively distracting stimuli during working memory performance [73].

On each trial, six capital letters are presented for 1500ms and participants are asked to memorize them. The presentation of the letters is followed by a delay period of 2000 ms, and

the presentation of another single letter. Participants have to decide whether or not the single letter was part of the initial block of letters. During the delay period, participants are either presented with a blank screen, a neutral or a negative picture. All picture stimuli are taken from the International Affective Picture System (IAPS) [74]. Neutral and negative IAPS stimuli are matched for social content and perceptual complexity.

The ability to control interference from irrelevant information will be examined by comparing response latencies between blank screens, neutral, and negative stimuli presented in the delay period.

Stroop Paradigm

The Stroop task is based on a paradigm by Etkin and colleagues [75 76] and measures the ability to control interference from simultaneously presented irrelevant information.

Each trial consists of the presentation of a happy or an angry facial expression with the word "Anger" or "Happiness" printed across the facial expression. Participants are asked to ignore the words and to indicate by button press whether the face picture displays an angry or happy facial expression. Facial expressions and words are either congruent or incongruent. Each picture/word combination is presented for 1000 ms. All facial expressions are taken from the original Ekman faces set [77].

The ability to control interference from irrelevant information is assessed by the classical behavioral interference effect (i.e. response latencies to incongruent trials as compared to response latencies to congruent trials). In addition, trials can be classified based on the congruence of the previous trial: congruent trial following a congruent trial (cC), incongruent trial following a congruent trail (cI), congruent trial following an incongruent trial (iC), and incongruent trial following an incongruent trial (iI).

Additional Measures

Prediction and Recall of affect, sleep, and affect regulation strategies

In the first laboratory session, participants will be presented with all items from the ambulatory assessment (e.g., affect, affect regulation strategies, sleep) and asked to indicate on a scale from 0 (not at all) to 7 (very much) how much they expect to feel or behave this way (on average) during the following seven days. At the end of the ambulatory assessment period, participants will be presented with all items from the ambulatory assessment again and asked to indicate on a scale from 0 (not at all) to 7 (very much) how much they had felt or behaved this way (on average) during the past seven days.

Intelligence

Participants' intelligence will be estimated by assessing the subtest 4 of the Leistungsprüfsystem (LPS-4) [78]. This serves to control for group differences in basic cognitive capabilities when examining group differences in cognitive control.

Electrocardiogram

At the end of the second laboratory session, participants will be asked to put on an ECG chest belt to measure their resting state heart rate variability for a 5-minute period. Participants are asked to relax during the ECG assessment.

Movement

During the seven-day ambulatory assessment period, participants will be asked to wear an accelerometer attached to their hips. The accelerometer continuously assesses data regarding participants' acceleration in all three geometric axes, context temperature, and air pressure [79]. This will allow to examine individual levels of physical activity and energy expenditure during the ambulatory assessment period.

Procedures

The procedure of this project is depicted in Figure 1. Data collection started in 01/2017 and will last till the end of 2018.

Sample size determination

Power analysis for group differences in cognitive control

Previous studies examining impairments in valence-dependent cognitive control in depressed compared to control participants yielded medium between group effect sizes (WMST task: e.g., d=0.78) [38]. Similar effect sizes were obtained for group differences in valence-dependent cognitive control between individuals with BPD and healthy controls (interference control: e.g., d=0.89) [34]. To detect medium sized group differences in cognitive control functions using univariate ANOVAs, a total sample size of N=159 (N=53 per group) is needed as determined using G*Power (assuming α=.05, power of .8). For selected post-hoc group comparisons, a group size of N=51 is required (assuming α=.05, power of .8, allocation ratio = 1). Note, that we will use multi-level modeling to test group differences in cognitive control. Given that multi-level modeling includes several assessment points per individual, the intended sample size of N=159 will be more than sufficient to detect medium sized group differences in cognitive control using multi-level modeling.

Power analysis for ambulatory assessment data

A sample size of N=159 that is required for the experimental part of the study is also large enough to ensure appropriate power for analyzing the ambulatory assessment data. For the ambulatory assessment part, all variables will be assessed 8 times a day for 7 consecutive days. For the multilevel analysis this would mean that there are 56 occasions of measurement nested within 159 individuals resulting in 8904 data points. For variable affective states it is reasonable to assume an intraclass correlation of 0.30 resulting in a design effect of DE = 21.7

[80]. Therefore, our multilevel analysis would be approximately comparable to a classical multiple regression analysis with 410 individuals [80]. Given this sample size it would be possible to detect a small interaction effect between two independent variables (partial R2 = 0.01) in a multiple regression analysis with a power of .8 (assuming α=.05).

Data analysis

1. Affective dynamics

To assess whether groups differ in their affective dynamics (i.e., inertia, instability, variability), we will calculate three different within-person measures for both positive and negative affect [81]: (a) Affective variability will be assessed by the within-subject standard deviation of the respective affect scale. (b) Affective instability will be calculated as the within-subject root Mean Square Successive Difference (rMSSD) between consecutive affect measures. (c) Inertia will be assessed by the temporal dependency of consecutive affect measures, i.e., the within-subject lag-one autocorrelation. Autocorrelations will be Fisher's z transformed to normalize their distribution.

Based on the distribution of the respective indices, we will select adequate methods for testing group differences. We will further examine whether controlling for mean levels of positive or negative affect will have an impact on the main effect of Group [82].

2./3. Group differences in the use and effectiveness of affect regulation strategies

To examine whether groups differ in the frequency of using rumination, suppression, or reappraisal, we will employ hierarchical linear modeling. The dependent variable will be the intensity rating of the respective AR strategy assessed at time t. The predictor variable of interest will be Group (BPD, MDD, CTL). In addition, we will enter the intensity rating of all other strategies to control for overall AR strategy use.

To examine whether the effectiveness of rumination, suppression, or reappraisal differs among groups, we will employ hierarchical linear modeling. The dependent variable will be the respective affect rating (positive or negative) at time t. Affect ratings at time t-1 will be entered as predictor. Predictor variables of main interest will be Group (BPD, MDD, CTL) and the intensity of each assessed AR Strategy (reappraisal, rumination, suppression, distraction, acceptance, social sharing) employed between time t-1 and time t.

4. Group differences in cognitive control functions

Reaction time data from the behavioral experiments will be cleansed according to the following procedures: outliers in response latencies will be defined as values below or above the upper or lower fences of each individual's distribution in each experimental condition. Outliers will be eliminated. In addition, participants will be excluded from analyses if their overall accuracy level indicates that the task was not sufficiently understood.

In a first step, group differences in cognitive control functions will be analyzed using separate multi-level models per experiment. Response latency will be the dependent variable. The Experimental Condition, Stimuli Valence (where applicable), and Group will be entered as predictor variables.

In a second step, composite scores for the ability to discard irrelevant information from working memory, and for the ability to control interference from distracting information will be generated. Group differences on these composite scores will be examined by using multi-level models. The respective composite score will be the dependent variable. Stimuli Valence and Group will be entered as predictor variables.

5. Relating cognitive control functions and affect regulation

a. To examine whether the *use* of rumination, suppression, or reappraisal will be related to individual differences in cognitive control functions, we will employ hierarchical linear

modeling. The dependent variable will be the intensity rating of the AR strategies assessed at time t. The predictor variables of interest will be the specific Strategy (reappraisal, rumination, suppression, distraction, acceptance, social sharing), and the Cognitive Control scores, as detailed below.

b. To examine whether the *effectiveness* of reappraisal, rumination, or suppression will be related to individual differences in cognitive control functions, we will also employ hierarchical linear modeling. The dependent variable will be the respective affect rating (positive or negative) at time t. Affect ratings at time t-1 will be entered as predictor variable (see 2./3.). Further predictor variables of interest will be Group (BPD, MDD, CTL), the Cognitive Control scores (see below), and the Intensity of each assessed AR strategy (reappraisal, rumination, suppression, distraction, acceptance, social sharing) employed between time t-1 and time t.

Cognitive control indices for each experiment will be computed as follows: For the 'Working Memory Selection Task', the discarding index will be computed as the median response latency to suppress probes minus the median response latency to novel probes of the same valence. Two separate difference scores, one for each valence condition (positive, negative), will be computed.

For the Removal and Updating task, the removal index will be assessed as the difference in response latencies between trials with short and long CTIs. This difference will be computed as a proportional gain score accounting for general processing speed (i.e., Removal Speed = [mean(short CTI) – mean(long CTI)] / mean(short CTI)). We will calculate two separate removal time indices for the removal of negative and positive words, respectively.

For the Stroop Task, the classical behavioral interference effect (i.e. response latencies to incongruent trials minus response latencies to congruent trials) will be computed.

In the 'Delayed Working Memory Task', a general distraction score will be computed by subtracting response latencies in trials with blank screens presented in the delay period from response latencies in trials with neutral and negative IAPS stimuli presented in the delay period. In addition, we will calculate an 'affective distraction score' by subtracting response latencies for neutral stimuli from response latencies for negative stimuli.

Patients and public involvement

There was no further involvement of patients or the public in the development of this study protocol. The results of this study will be forwarded to interested participants. Results will be disseminated to relevant psychotherapeutic and patient communities in peer-reviewed journals, and at scientific conferences.

Ethics and dissemination

The study has been approved by the Ethics Board at Freie Universität Berlin, Germany (No.: 67/2013; Amendment: 136/2017) and will be conducted in accordance with the Helsinki Declaration. The research team members have made sure that the study respects the following ethical principles: all the personal data gathered will be treated confidentially, written informed consent will be collected, data will be securely stored, and the data will only be used for research purposes. Participation in this research study is voluntary. Participants will be reminded of their rights to withdraw from the study without giving any reason. Data privacy will be guaranteed: all the research data gathered during the project will be identified using pseudonyms. Personal data will be kept under lock and is stored separately from research data. Communications and publications will not enable identification of individual participants. Ambulatory assessment will be realized with a smartphone application (movisensXS) on devices provided by the research team. No further information of the participants' behavior (e.g., GPS-tracking of movement profiles) is stored.

We plan to publish several articles in peer-reviewed scientific journals. In addition, we will communicate the results at scientific congresses. This research project will also result in a PhD thesis.

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Figures

Figure 1. Procedure of the research project

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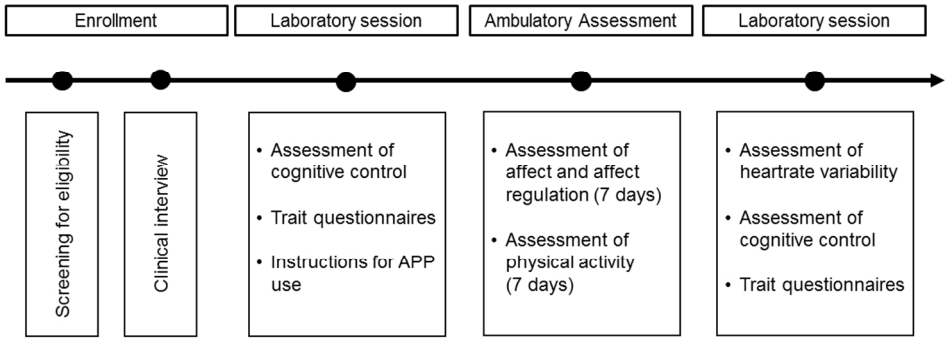
Conflict of Interests

All authors declare that there are no conflicts of interest.

Contributorship Statement

Lars Schulze and Ulrike Zetsche designed the study, wrote the funding grant, and drafted and revised the current manuscript. Paul Christian Bürkner was responsible for the data analytic plan, wrote the section data analysis, and revised the current manuscript. Julian Bohländer piloted the Removal and Updating task, coordinates the data assessment, and wrote and revised the current manuscript.



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