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CHAPTER 5

Imagine your mood: Study design and protocol of a randomized controlled micro-trial using app-based experience sampling methodology to explore processes of change during relapse prevention interventions for recurrent depression

Abstract
Relapse prevention strategies include continuation of antidepressant medication and preventive psychological interventions. This study aims to gain understanding that may inform tailoring of relapse prevention to individual differences, to improve their effects. Such treatment personalization may be based on repeated assessments within one individual, using experience sampling methodology. As a first step towards informing decisions based on this methodology, insight is needed in individual differences in risk of relapse and response to treatment, and how relapse prevention strategies may differentially target vulnerability for relapse.

The smartphone application ‘Imagine your mood’ has been developed specifically for this study to assess cognitions, imagery, emotions, and behaviors in daily life. Parallel to the randomized controlled trial ‘Disrupting the rhythm of depression’, 45 remitted recurrently depressed individuals taking continuation antidepressant medication will be randomly assigned to either continuing antidepressant medication (n = 15), continuing antidepressant medication combined with an eight-session preventive cognitive therapy (n = 15), or tapering of antidepressant medication in combination with preventive cognitive therapy (n = 15). Relapse and return of depressive symptomatology over a 24-month follow-up will be assessed. Additionally, matched never depressed individuals (n = 15) will be recruited as controls.

This innovative study combines the strengths of a randomized controlled trial and experience sampling methodology in a micro-trial to explore individual differences in risk of relapse and what works for whom to prevent relapse. Results may ultimately pave the way for therapists to tailor relapse prevention strategies to individual (affective) vulnerability.
BACKGROUND

Major Depressive Disorder (MDD) poses a heavy burden on patients and society (Ferrari et al., 2013; Greenberg, Fournier, Sisitsky, Pike, & Kessler, 2015; Whiteford et al., 2013). The highly recurrent nature of MDD (Burcusa & Iacono, 2007; Richards, 2011) adds greatly to the burden of depression (Judd, 1997; Riihimäki, Vuorilehto, & Isometsä, 2015). With every previous episode the risk of relapse increases, so that after having experienced two or more depressive episodes the chance of relapse is 60–90% (Eaton et al., 2008; Hardeveld et al., 2010; Moffitt et al., 2010). Reducing the burden of MDD therefore crucially involves prevention of recurrence in previously depressed individuals.

Although both continuation of antidepressant medication (ADM; Glue, Donovan, Kolluri, & Emir, 2010; Hansen et al., 2008) and psychological interventions (Biesheuvel-Leliefeld et al., 2015; Clarke, Mayo-Wilson, Kenny, & Pilling, 2015; Guidi, Fava, Fava, & Papakostas, 2011; Piet & Hougaard, 2011; Vittengl, Clark, Dunn, & Jarrett, 2007) can reduce the risk of relapse, many previously depressed individuals do relapse in the long run. Individual patients may differ in their vulnerability for relapse. Identifying these individual differences and understanding how different relapse prevention strategies target these vulnerabilities may enable therapists to further tailor interventions (Kazdin, 2016). Crucial questions therefore seem to be what works best for whom (Simon & Perlis, 2010; Uher, 2008). However, empirical evidence guiding such personalized relapse prevention strategies is scarce (Bockting et al., 2015). To date, attempts to identify single individual characteristics that determine treatment response have not resulted in consistent moderators of effect that may inform treatment decisions (Kazdin, 2016; Kuyken et al., 2016).

Experience Sampling Methodology (ESM; Csikszentmihalyi & Larson, 1987; Myin-Germeys et al., 2009; Shiffman et al., 2008) offers a route towards personalized interventions (van Os et al., 2017). By repeatedly assessing cognitions, emotions, and behaviors in the flow of daily life, ESM allows for assessment of their interrelations, temporal dynamics and change over time. Furthermore, integrating ESM in clinical practice may empower patients (Simons et al., 2015) and provide feedback to both patients and therapists, with positive long-term results (Kramer et al., 2014). Further advantages of ESM are minimization of retrospective biases, which may be particularly relevant in depression (Morris, 1999), and maximized ecological validity by
random sampling in daily life (Myin-Germeys et al., 2009). ESM may be ideally suited for informing and optimizing personalized treatments (Verhagen, Hasmi, Drukker, van Os, & Delespaul, 2016). However, for applying ESM to the individual patient, insight is needed in individual differences in vulnerability for relapse and early response to treatment. Also, understanding of the working mechanisms of different relapse prevention strategies is needed.

This report aims to describe the theoretical rationale and study design for ‘Imagine your mood’, an innovative study exploring the potential for using ESM for informing personalized relapse prevention. In the ‘Imagine your mood’ study, data of both previously depressed and matched never depressed individuals will be collected. ESM will be added to a three-arm relapse prevention trial ‘Disrupting the rhythm of depression’ (Bockting et al., 2011). This randomized controlled trial (RCT) investigates PCT while either continuing or tapering ADM as a relapse prevention strategy compared to continuation ADM in a sample of individuals diagnosed with remitted recurrent MDD.

**Theoretical rationale**

**Relapse prevention strategies**

Relapse prevention often consists of continuation of antidepressant medication (ADM) after the acute phase of depression (American Psychiatric Association, 2010). Meta-analyses show that ADM reduces risk of relapse (Glue et al., 2010; Hansen et al., 2008). However, many ADM users experience adverse side effects such as weight gain, sexual problems, and emotional numbing (Cartwright, Gibson, Read, Cowan, & Dehar, 2016; Kelly, Posternak, & Alpert, 2008). In addition, many ADM users have difficulty with long-term adherence to ADM (Bockting et al., 2008; ten Doesschate, Bockting, & Schene, 2009). Discontinuation of ADM may also be problematic as individuals who wish to discontinue or taper their ADM may be hampered by withdrawal symptoms (Fava, Gatti, Belaise, Guidi, & Offidani, 2015) and discontinuing their ADM may leave them more vulnerable to relapse (Dobson et al., 2008; Hollon, Stewart, & Strunk, 2006; Vittengl et al., 2007).

Most patients prefer psychological treatment strategies (Prins, Verhaak, Bensing, & van der Meer, 2008; van Schaik et al., 2004). Several psychological interventions have been developed specifically for preventing relapse in depression, i.e. preventive cognitive therapy (PCT; Bockting et al., 2005), mindfulness-based cognitive therapy (MBCT; Teasdale et al., 2000),
and wellbeing cognitive therapy (Fava, Rafanelli, Grandi, Conti, & Belluardo, 1998). Meta-analyses conclude that preventive psychological therapies reduce risk of relapse (Biesheuvel-Leliefeld et al., 2015; Clarke et al., 2015; Guidi et al., 2011; Piet & Hougaard, 2011; Vittengl et al., 2007), possibly even more than continuation of ADM after the acute phase of depression does (Biesheuvel-Leliefeld et al., 2015). Recently, two randomized controlled trials (RCTs) have examined whether one of these psychological interventions (MBCT) may be a viable alternative to continuation of ADM for preventing relapse in depression. These studies show mixed results. Kuyken et al. (2015) found no difference in relapse rates within 24 months for a group of remitted recurrently depressed participants that continued ADM (49%, n = 212) compared to a group that received MBCT with ADM tapering (44%, n = 212). Huijbers et al. (2016), however, found significantly higher relapse rates (over 15 months) for the group that received MBCT and tapered ADM (54%, n = 128) versus the group that received MBCT and continued ADM (39%, n = 121).

Thus, although both continuation of ADM (Glue et al., 2010; Hansen et al., 2008) and psychological interventions (Biesheuvel-Leliefeld et al., 2015; Clarke et al., 2015; Guidi et al., 2011; Piet & Hougaard, 2011; Vittengl et al., 2007) can reduce the risk of relapse, many previously depressed individuals do relapse in the long run.

**Experience Sampling Methodology**

ESM data can be used to model temporal dynamics and individual networks in accordance with a network perspective on depression. In this perspective, depression is conceptualized as a complex dynamical system of interacting symptoms, cognitions, emotions, and behaviors (Cramer et al., 2016; Hayes, Yasinski, Barnes, & Bockting, 2015). Relapse may then be conceptualized as a transition of the network into a depressive state (Hosenfeld et al., 2015). Given that depression is highly heterogeneous (Fried & Nesse, 2015), these networks may vary greatly between individuals and ESM may be used to construct personalized networks. These individual networks potentially contain indicators of vulnerability for relapse, including early warning signals of relapse within an individual (van de Leemput et al., 2014).

A body of empirical literature is rapidly emerging that supports the potential for ESM to contribute to personalizing interventions in depression (Verhagen et al., 2016). First, preliminary studies support the hypothesis that ESM provides information on vulnerability for relapse. Recently, temporal
dynamics of affect have been hypothesized to signal sudden transitions into and out of a depressive state. Indeed, higher inertia (the degree to which current states can be predicted from previous states) was found in individuals at the brink of relapse (van de Leemput et al., 2014). Higher inertia of negative affective in particular is hypothesized to signal relapse (van de Leemput et al., 2014). Crucially, increased inertia within an individual may be an early warning signal of relapse. First evidence of such increased inertia was demonstrated in a previously depressed individual that attempted to taper his ADM (Wichers et al., 2016). The generalizability of this single case study is limited and requires replication. However, these findings demonstrate that individual networks may contain information about vulnerability for relapse. Further insight is needed in individual differences in these vulnerabilities.

Second, ESM allows for in-depth analyses of interrelations between cognitive mechanisms and affective vulnerabilities for relapse. For example, an ESM design was used previously to examine the hypothesis that the negative affective impact of rumination contributes to depressive symptomatology (Pasyugina, Koval, De Leersnyder, Mesquita, & Kuppens, 2015). Another mechanism of interest is mental imagery, frequently described as “seeing with the mind’s eye” (e.g. Kosslyn et al., 2001). Mental imagery has been related to stronger emotional responses to positive and negative stimuli (Holmes & Mathews, 2005; Holmes et al., 2008). However, it is unclear how mental imagery influences affect dynamics in daily life. Thus, ESM may elucidate mechanisms that underlie vulnerability for relapse within a group of previously depressed individuals.

Third, ESM may be used to monitor early responses during different treatment strategies that may predict whether an individual will benefit from a treatment. The previously mentioned single case study (Wichers et al., 2016) suggests that ESM may be used to monitor such early responses in individuals using different relapse prevention strategies. In acute depression, early changes in affect were found predictive of treatment outcome (Geschwind et al., 2011). Affective disturbances may play a central role in the depressive network (Fried, Epskamp, Nesse, Tuerlinckx, & Borsboom, 2016), given that depression is an emotional disorder (American Psychiatric Association, 2013). The importance of affect after remission as a risk factor for depressive relapse is supported by the finding that mood as assessed using a one-item visual analogue scale (VAS) running from happy to sad has been found predictive of relapse (van Rijsbergen et al., 2015) even after five and a
half years (van Rijsbergen et al., 2012). ESM may capitalize on this predictive value of affect, by examining whether early affective changes indicate whether an individual will for example be able to successfully taper ADM. However, whether early affective changes predict treatment outcome of different relapse prevention strategies has not yet been examined.

Fourth, ESM may provide new insights on potential mechanisms by which treatment strategies prevent depressive relapse. Psychological interventions and ADM may target vulnerability for relapse in different manners. This was first illustrated with ESM data in a study that investigated the effect of MBCT for individuals with residual depressive symptomatology. Using ADM during MBCT facilitated decrease in negative affect, but hampered increase in positive affect (Bakker et al., 2016). However, causal inferences based on this study are limited because the use of ADM was not randomly assigned. This study demonstrates that ESM may be used for uncovering differential pathways by which relapse prevention strategies may target affect in daily life. These differential effects of relapse prevention strategies may ultimately be used for tailoring interventions to individual affective vulnerability.

In sum, there are at least four routes to furthering personalized relapse prevention using ESM: exploring individual differences in vulnerability for relapse, examining (cognitive) mechanisms that contribute to (affective) vulnerability, interpreting early changes in response to treatment, and examining what mechanisms are differentially targeted by relapse prevention strategies.

**AIMS AND HYPOTHESES**

The first aim of the ‘Imagine your mood’ study is to explore individual differences in vulnerability for future relapse. In addition to exploring between-individual differences, within-individual affective change will be explored as a potential precursor for relapse. It is hypothesized that within-individual increases in negative affect and negative affective inertia may precede relapse. It will be examined whether such individual affective trajectories are specific to individuals at high risk of depressive relapse by examining these in a never depressed control group as well. By comparing ESM data of previously depressed and never depressed individuals, affective disturbances that may constitute vulnerability for depressive relapse will be explored. Second, how cognitive mechanisms interact with affective vulnerability for relapse will be examined. Specifically, how mental imagery is related to affect in daily
life will be investigated. Third, it will be examined whether early affective changes may be associated with successful tapering of ADM. It is hypothesized that affective improvements in the first two weeks of tapering may be associated with successful tapering of ADM. Fourth, it will be explored how relapse prevention strategies may differentially target vulnerability for relapse by group-based comparison of the networks in the three arms of the RCT. Finally, several secondary outcome measures will be included for hypothesis-generating purposes. In sum, this study combines the strengths of an RCT and ESM in a micro-trial to explore processing of change during different relapse prevention strategies.

**Study design**

This study is designed as a micro-trial that includes ESM to explore processing of change during different relapse prevention strategies. Participants ($N = 45$) will be randomly allocated to either continuing ADM ($n = 15$), continuing ADM combined with an eight-session PCT ($n = 15$), or tapering of ADM in combination with PCT ($n = 15$). Current and previous depressive episodes will be monitored using telephonic interviews at the start of the study and after three, nine, 15, and 24 months. The ESM procedure will take place during the first eight weeks of the study (parallel to the PCT training for those individuals randomly allocated to receive PCT). Data of a never depressed control group will be collected.

The addition of ESM to the RCT ‘Disrupting the rhythm of depression’ (Netherlands Trial Register: NTR1907) was approved by the medical ethical board of the University Medical Center Groningen (METc 2009/158). Ethical approval for including never depressed individuals has been obtained from the University of Groningen Ethical Committee of the Psychology Department (ppo-014-043). This study is funded by ZonMW: The Netherlands Association for Health Research and Development (171002401 and OOG Grant 100002035) and by NWO, the Netherlands Organization for Scientific Research (022.003.038).

**Sample**

The previously depressed sample will be recruited parallel to the three-armed RCT ‘Disrupting the rhythm of depression’ (Bockting et al., 2011). To be included, participants have to be diagnosed with remitted, recurrent MDD, as defined according to the Diagnostic and Statistical Manual of Mental Disorders (DSM–IV) and assessed by trained interviewers using the Structured
Clinical Interview for DSM–IV disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 1997). Further inclusion criteria are a current score of ≤10 on the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960), and use of continuation ADM in the last six months. Exclusion criteria are current mania or hypomania or a history of bipolar illness, any psychotic disorder (current and previous), organic brain damage, alcohol or drug dependency/abuse, and predominant anxiety disorder. After inclusion, participants will be randomly allocated to one of the three arms of the study.

The matched never depressed sample will be recruited via advertisements on social media, posters, and word of mouth. Participants will be selected to match the previously depressed sample on age, gender, and educational level. Exclusion criteria are current or previous depressive episodes as assessed with the SCID-I, and use of ADM. Participants will receive a 10 euro gift certificate.

**Procedure**

The procedure as described in the trial protocol of the RCT (Bockting et al., 2011) will be followed, with the adjustments that PCT will be administered individually rather than in groups, and the addition of the ESM procedure. Participants randomized to a PCT condition will receive eight weekly sessions of individual PCT, administered by trained psychologists using the treatment manual (Bockting, 2009). Participants randomized to ADM continuation (with or without PCT) will be advised to continue ADM in line with leading clinical guidelines (American Psychiatric Association, 2010; National Collaborating Centre for Mental Health, 2004) and their general practitioner or psychiatrist will also be informed. For participants randomized to the tapering condition, the instruction will be to gradually taper ADM in four weeks guided by their general practitioner or psychiatrist, who will also be informed and advised.

**Smartphone application ‘Imagine your mood’**

The experience sampling app ‘Imagine your mood’ has been developed and programmed using TEMPEST software (Batalas & Markopoulos, 2012). This app will enable participants to fill out the questionnaires on their own smartphone. If needed, a research-smartphone will be made available to participants. The questionnaire includes a section on affect and emotions, followed by questions about cognitions and imagery, and finally a section on activities. The application has been programmed to set triggers for questionnaires ten
times a day, three days a week (on Thursdays, Fridays, and Saturdays), for eight weeks, resulting in a maximum of 240 responses. The triggers are set semi-randomly, with one trigger per 90-minute interval between the hours of 7.30 and 22.30, and a minimum of 30 minutes between triggers.

During an approximately one-hour face-to-face briefing, a trained assistant will install the app on the smartphone of a participant, explain the ESM procedure, elucidate the more difficult concepts, help practice the questionnaire, and answer any questions. Participants will be instructed to respond to a trigger as soon as possible, and answer the questionnaire about the moment just before the trigger. Participants will not be informed about the five-minute time limit that is set on the questionnaire; they will be instructed that they are too late if the questionnaire is no longer available. Participants will receive weekly brief structured telephonic interviews to monitor the functionality and use of the ‘Imagine your mood’ app. Participants will be invited to contact their assistant for questions or technical difficulties. An overview of assessments is provided in Table 5.1.

MEASURES

Affect

Momentary mood will be assessed with the mood scale (van Rijsbergen et al., 2012). Participants rated the question “at the moment, I feel...” on a VAS ranging from happy (0) to sad (100).

Table 5.1
Overview of assessments

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Baseline</th>
<th>ESM study period</th>
<th>Follow-up period (in months)</th>
<th>3</th>
<th>9</th>
<th>15</th>
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<td>SCID-I</td>
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<td>ESM</td>
<td>+ (8 weeks)</td>
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<tr>
<td>Weekly calls</td>
<td>+ (8 weeks)</td>
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Note. ESM = Experience sampling methodology, + Both previously depressed and never depressed individuals, * Previously depressed individuals only.
Adjectives to assess positive affect and negative affect were selected based on previous research (e.g. Wichers et al., 2015) and the adjectives described in the diagnostic criteria of a depressive episode (American Psychiatric Association, 2013), and discussions in our research team. Ratings of the adjectives (on a 0–100 VAS) will be averaged to a positive affect (cheerful, enthusiastic, hopeful, content, energetic) and a negative affect (anxious, angry, lonely, irritated, down, suspicious, helpless, guilty, insecure) scale per moment per individual.

**Degree of mental imagery**
First, participants will be presented with instructions to identify what they had in mind just before the trigger, i.e. their mental representation. In the briefing, participants will be familiarized with this procedure and instructed as follows “you (almost) always have something in mind. Please take your time to recall what you had in mind just before the trigger. If you do not remember what you had in mind just before the trigger, please select the most recent thing you had in mind that you can remember.”

Participants will receive the following information about mental imagery: “Sometimes you see things in mind, while you do not see those with your eyes at that moment. For example, when you recall a memory or when you imagine yourself doing something in the future. You can also experience this with other sensory modalities. With hearing, for example, when you have a song in your head. Can you for example remember the last time you did groceries, or that you were on vacation? What do you see in your mind’s eye? Can you hear the sounds in the memory? Or feel a physical sensation, like the sun on your face or perhaps an itch?”

Participants will rate the degree of visual mental imagery answering the question “I see it in my mind’s eye” on a VAS running from 0 to 100. Non-visual mental imagery will be assessed with the questions “(it) is an auditory sensation,” and “(it) is a physical sensation.”

Participants will rate the valence of their mental representation on a VAS ranging from negative (0) to positive (100).

**Follow-up measures (for previously depressed participants only)**
The primary outcome measure of the ‘Disrupting the rhythm of depression’ RCT (Bockting et al., 2011) is the time-related proportion of depressive relapse as assessed using the SCID-I at three, nine, 15 and 24 months (current depressive symptomatology and previous three, six, or nine months).
Severity of depressive symptomatology at all time points will be assessed with the HRSD.

*Successful tapering of ADM (for previously depressed participants only)*

The ADM dose will be assessed during the weekly telephonic interviews. Both a lenient and a stringent operationalization of successful tapering will be used. The lenient operationalization entails an ADM dose reduction of $\geq 0\%$, whereas the stringent operationalization additionally requires that the individual does not relapse into a depressive episode.

**MEASURES FOR HYPOTHESIS-GENERATING PURPOSES**

*Impact of ESM*

Additional measures will be included in the questionnaire to explore whether responding to the ‘Imagine your mood’ app may have an impact on affect. After reporting on their emotions and mental representation just before the beep, participants will be asked to assess their current mood on a VAS ranging from happy (0) to sad (100) and their current anxiety (0–100). Furthermore, at the end of the questionnaire participants will be asked to what degree filling out the questionnaire had bothered them (on a 0–100 VAS).

*Mental representation*

For exploratory reasons, several other aspects of the selected mental representation (what I have in mind...) will be assessed (on 0–100 VASs). Concrete verbal thinking will be assessed with the questions “I think in words” and “I think in sentences.” Abstract verbal thinking (worry/rumination) has been included in the questionnaire using the following items: “I’m worrying,” “I think about my feelings,” “I wonder why I react the way I do,” and “I analyze the meaning of my feelings.” The intrusiveness will be assessed using the adjectives derived from Brewin et al. (2009): “distressing,” “uncontrollable,” “interfering,” and “vivid.”

Additionally, participants will be asked to rate the degree to which the mental representation is personally relevant (0 = not personally relevant, 100 = personally relevant), whether it refers to “the distant past” (0) or “the far future” (100), and whether they experience the tendency to approach (0) or avoid (100) what they had in mind. Momentary avoidance tendencies will be calculated by averaging this last rating with the rating on the question as to what degree they experience the tendency to approach (0) or avoid (100) their emotions.
Physical complaints
Physical complaints will be assessed with the questions “I feel tired” and the recoded “I feel fit physically” (on 0–100 VASs).

Activities
Participants will be asked to identify their current activity and rate this activity on the following scales: “I like doing this,” “this activity requires effort,” “I feel I’m being active” (on 0–100 VASs) and select the category to which the activity belongs.

Participants will be asked to select the most important previous activity (stressor or event) in the two hours before the trigger, rate this activity on a VAS that runs from “unpleasant” (0) to “pleasant” (100), and select the category to which the activity belonged.

Finally, participants will be invited to identify the most important future event in the next two hours, answer the question “I’m not looking forward to it” (lack of anticipatory pleasure) on a 0–100 VAS and select the category to which the event belongs.

Analyses
Different analyses will be used for the variety of research questions. The experience sampling data represent repeated measurement within individuals, and this nested structure will be taken into account in all the analyses. An important assumption in many time series analyses is stationarity (i.e. that processes do not change over time). This assumption will be handled either by removing the trends from the data, or by using analyses that do not assume stationarity. Baseline characteristics of never depressed and previously depressed individuals will be compared to examine whether confounding factors may play a role.

First, individual differences in affect will be explored. For examining whether affective changes may signal future relapse, time-varying autoregressive time series models (Bringmann, Hamaker, Aubert, Borsboom, & Tuerlinckx, 2016) will be fitted for each individual. These models allow for the processes in the data to change over time and are excellently suited for examining the presence of such time-varying processes within individuals. Specifically, the presence of changes in the intercept and autoregressive parameter (see Equation 5.1) are examined to assess the presence of change in mean level and inertia of negative affect. These analyses will be performed
both in previously depressed and in never depressed individuals, to examine whether individual affective trajectories are specific to depressive relapse.

\[ \text{Negative affect}_t = \beta_0 + \beta_1 \text{Negative affect}_{t-1} + \epsilon_t \]  

(5.1)

Second, how imagery-based processing may contribute to affective disturbances in daily life will be explored using mixed linear models. Trends over time will be removed from the data to prevent spurious correlations and data will be person-mean centered. Post-hoc analyses will be used to examine whether findings hold in both the previously depressed and never depressed groups.

Third, it will be examined whether early affective responses can predict successful tapering of ADM by analyzing the data of the first two weeks in the previously depressed participants randomized to PCT while tapering ADM. A bivariate vector-autoregressive Bayesian dynamic model (Krone, Albers, Timmerman, 2016) will be performed to model the time structure of the data. More specifically, the mean levels, inertia, and variability will be assessed. Subsequently, it will be examined how these measures of affect and affect dynamics are related to successful tapering of ADM.

Finally, network modeling will be used in two exploratory ways to examine whether relapse prevention strategies in the three treatment arms of the RCT differentially target the network of dynamic interactions between cognitive, behavioral, and affective states. First, group-level network analyses will be used to investigate potential differences in network architecture (e.g., centrality) between the three arms of the trial. Second, as intra-individual network modeling in the context of clinical trial data is still in the developing phase, it will be explored to which extent changes in network architecture over time within individuals can be assessed.

**Discussion**

Both continuation of ADM and psychological interventions can reduce the risk of relapse in previously depressed individuals, but knowledge informing what works best for whom is needed. This micro-trial aims to explore how ESM may inform personalized relapse prevention strategies. Emotions, mental imagery, cognitions, and behaviors will be repeatedly assessed using the smartphone application ‘Imagine your mood’ in a group of previously depressed individuals. The data will be collected alongside a three-armed RCT
‘Disrupting the rhythm of depression’ that investigates what works best in preventing relapse (i.e. continuation of ADM, the combination of ADM with PCT, or tapering ADM combined with PCT). Additionally, a control group of matched never depressed individuals will be included. The relatively limited number of participants included in this micro-trial (45 previously depressed and 15 matched never depressed individuals) will be compensated by the great number of repeated assessments (max 240) within each individual.

In sum, this study will explore four routes to furthering personalized relapse prevention using ESM: individual differences in vulnerability for relapse, processes underlying affective vulnerability, within-individual change while undergoing different relapse prevention strategies and how these relate to successful tapering and prevention of relapse, and differential effects of relapse prevention strategies. These four approaches may be interdependent. For example, examining how cognitive mechanisms contribute to affective vulnerability may be complemented by an understanding of how mechanisms are targeted by different relapse prevention strategies. The data may help unravel the role of individual differences in depressive relapse while undergoing different relapse prevention strategies. This may provide novel information on processes of change as a first step towards improving the protective effect of relapse prevention strategies by tailoring them to individual needs using experience sampling methodology.
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