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The intra-day dynamics of affect, self-esteem, tiredness, and suicidality in Major Depression

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ABSTRACT

Despite growing interest in the temporal dynamics of Major Depressive Disorder (MDD), we know little about the intra-day fluctuations of key symptom constructs. In a study of momentary experience, the Experience Sampling Method captured the within-day dynamics of negative affect, positive affect, self-esteem, passive suicidality, and tiredness across clinical MDD ($N = 31$) and healthy control groups ($N = 33$). Ten symptom measures were taken per day over 6 days ($N = 2231$ observations). Daily dynamics were modeled via intra-day time-trends, variability, and instability in symptoms. MDD participants showed significantly increased variability and instability in negative affect, positive affect, self-esteem, and suicidality. Significantly different time-trends were found in positive affect (increased diurnal variation and an inverted U-shaped pattern in MDD, compared to a positive linear trend in controls) and tiredness (decreased diurnal variation in MDD). In the MDD group only, passive suicidality displayed a negative linear trend and self-esteem displayed a quadratic inverted U trend. MDD and control participants thus showed distinct dynamic profiles in all symptoms measured. As well as the overall severity of symptoms, intra-day dynamics appear to define the experience of MDD symptoms.

1. Introduction

Recent research has found that dynamics in affect are an integral part of depression (Houben et al., 2015; Pe et al., 2015). This has led to calls for affective dynamics to be included in the diagnostic criteria for Major Depressive Disorder (MDD; Bowen et al., 2013). It would follow that other MDD symptoms are dynamic in nature, and that these dynamics are as important as overall symptom levels or intensity. However, very little research exists on the within-day dynamics of MDD symptoms other than affect. This study aims to obtain a descriptive picture of the daily fluctuations and rhythms of a range of symptom constructs in MDD.

By its very nature, MDD is a dynamic construct: symptoms are known to change over time, with MDD episodes fluctuating across remission, pro-dromal, and more clinically severe periods at different points over months and years (Fried et al., 2016; Iacoviello et al., 2010; Vergunst et al., 2013). Theory also suggests that depressive symptoms fluctuate at a more micro-level: for example, cognitive-behavioral as well as more recent work suggests that depressive symptoms are activated on a moment-to-moment basis over the course of daily life (Beck et al., 1979; Wichers, 2014). Alterations in the circadian rhythms of biological processes such as cortisol and melatonin secretion have also been found to be associated with depression (Peeters et al., 2003; Sundberg et al., 2016). Research and theory on the factors underlying MDD therefore outline inherently dynamic processes that occur within the context of an individual's everyday life. However, to date, research on MDD symptoms has relied mostly on measures and diagnostic conceptualizations of MDD that do not capture the daily flow of MDD experience.

We use the Experience Sampling Method (ESM; Csikszentmihalyi and Larson, 1987; Stone and Shiffman, 1994) to empirically assess the intra-day dynamics of five key MDD symptom dimensions (adapted to the momentary micro-level from macro-level DSM / ICD diagnostic criteria) in a sample of MDD and healthy control participants. At the

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macro-level, MDD is not a unidimensional construct; rather, it is a syndrome comprised of heterogeneous symptoms that are distinct etiologically and have differential effects on biopsychosocial functioning (Fried et al., 2016; Fried and Nesse, 2014). Indeed, an in-depth symptom-level approach to MDD research has recently been proposed (Fried and Nesse, 2015). Macro-level symptoms are expressions of micro-level, moment-to-moment symptom experience (Wichers, 2014). In the present study, we therefore study micro-level symptoms separately, rather than as part of one construct. Alongside positive affect (PA) and negative affect (NA), the dynamics of self-esteem, tiredness, and suicidality are explored. These symptoms include cognitive and affective symptoms, as well as a somatic, non-affective symptom (tiredness). These symptoms were chosen as the focus of study over others (e.g. appetite changes, psychomotor symptoms, and concentration difficulties) because they have been the focus of previous ESM research. As such, they have all been found to have within-day fluctuations and are known to be subjective experiences that can be studied effectively with ESM.

1.1. Conceptualizing ‘dynamics’ and their operationalization in affect

This study conceptualizes the temporality of symptoms in three ways, as: (1) variability in symptom scores across the sampling period; (2) instability in symptom scores between moments; and (3) systematic trends in hour-by-hour symptom levels. Below, each conceptualization is defined and a brief summary is given of how such measures have been operationalized in relation to affect in MDD.

1.1.1. Defining variability and instability

These concepts are defined comprehensively elsewhere (see Houben et al., 2015 and Jahng et al., 2008). In short, symptom variability captures the overall spread of an individual's symptom scores across a sampling period (i.e. intra-individual variance or standard deviation). Instability is a more temporally contingent measure, capturing the frequency and amplitude of symptom fluctuations between moments. It is the within-person *successive difference* in between-moment symptom scores.

1.1.2. Affect variability and instability

The extent to which affect fluctuates during the day is a central part of subjective emotional experience. In the past decade, a body of research has found that greater variability and instability in NA are related to poor psychological well-being in general and MDD in particular (Houben et al., 2015; Wichers et al., 2010).

The relationship between PA instability/variability and MDD is less clear. In their meta-analysis, Houben et al. (2015) found that although PA variability/instability was positively associated with poorer psychological health, it was a less powerful predictor of this than NA variability/instability. Studies on clinical populations have typically found no significant association between PA variability/instability and MDD (Peeters et al., 2006; Thompson et al., 2012). Indeed, when the Houben et al. meta-analysis was confined to studies with clinical populations, MDD was actually associated with *less* variability (though not instability) in PA.

Given that depression is thought to be a dimensional construct (Prisciandaro and Roberts, 2005), it is not clear why studies have found that increased PA instability and variability are associated with depressive symptoms in the general population, but not with depression diagnosis in clinical populations (Gruber et al., 2013; Houben et al., 2015). Indeed, Houben et al. describe their finding that less variability in PA is associated with clinical depression as ‘anomalous’, while also suggesting that less PA variability may reflect the MDD experience of anhedonia and resulting lack of PA reactivity. The research in that review includes studies using different methodologies (e.g. both ESM and retrospective measures), different time-scales between reports (between-day reports and intra-day reports) and different calculations of variability/instability (e.g. multilevel vs. single level variability/instability analyses). Given these marked methodological and measurement differences, a coherent body of research on intra-day, hour-to-hour PA variability/instability in MDD has not yet formed. Indeed, the number of studies that have explored intra-day variability/instability in affect in MDD remains relatively small. As a result, the nature and relative importance of PA and NA variability and instability in MDD is unclear. Further research on clinical samples using fine-grained, multilevel ESM methods is needed to clarify these matters.

1.1.3. Defining diurnal time-trends

Neither variability nor instability directly account for how time itself may influence symptom levels. In contrast, the time-trend approach models symptom severity as a function of time of day. It identifies any systematic patterns of change in symptom levels across the day. Just as research on biological circadian rhythms has shown that certain circadian patterns are associated with disease outcomes (Takahashi et al., 2008), so too may diurnal rhythms in psychological experience play a key role in functioning and outcomes in depression.

1.1.4. Diurnal time-trends in affect

Relatively little research exists on diurnal affective rhythms in MDD (indeed, diurnal time-trends were not included in the Houben et al. (2015) meta-analysis of affect dynamics). Traditional clinical descriptions of MDD incorporate a ‘morning-worse’ pattern in affect (Hall et al., 1964; Leibenluft et al., 1992). However, the few studies that have systematically investigated diurnal time-trends in affect have yielded conflicting results.

One ESM study found a ‘morning-worse’ pattern in both NA and PA (Peeters et al., 2006). MDD participants exhibited an inverted U-shaped pattern in NA with a peak in the mid-morning, while the NA of control participants did not exhibit a diurnal trend. PA displayed an inverted U-shaped pattern in both groups. MDD participants, however, showed a significantly steeper slope in PA over the day, with relatively lower morning and higher evening levels. These findings are similar to those of Daly et al. (2011), where individuals with high levels of psychological distress had a more pronounced diurnal affective rhythm than those with low distress levels, characterized by much lower morning PA and somewhat higher morning NA. In contrast, Murray (2007) found a *less* distinct diurnal quadratic rhythm in PA in individuals with high depression levels compared to those with low depression levels. NA was not found to have a time-trend in either group. Mata et al. (2012) found no differences between MDD and control groups in the time-trend of either NA or PA.

Peeters et al. (2006) is the only study we are aware of that used a clinical MDD sample in its investigation of time-trends. Mata et al. (2012) used a community sample that was diagnosed with/without MDD using structured clinical interviews, while both Murray (2007) and Daly et al. (2011) used non-clinical samples (indeed, while the PA time-trend differed across high and low depression scorers in Murray (2007), mean levels in PA were not significantly different between groups). The nuances of differences in diurnal patterns of affect may only be apparent in individuals with clinically more severe MDD. Further research on clinical samples is therefore needed to establish a consensus on the daily affective time-trend of MDD.

1.2. The intra-day dynamics of self-esteem, suicidality, and tiredness in MDD

Taken together, research on the intra-day dynamics of affect strongly suggests that dynamic change is a core characteristic of MDD. It emphasizes the need to move beyond static conceptualizations of affect, where an individual's average levels are the only aspect considered. The dynamics revealed by these studies point to increased emotional fluctuations in MDD and difficulties in regulating daily subjective experience. It follows that other key MDD symptoms – such as self-esteem, suicidality and tiredness – may also be characterized by specific dynamic patterns. However, as discussed below, research has continued to focus on absolute levels of these symptoms in MDD and has not yet considered in detail the nature and pattern of their intra-day fluctuations.

1.2.1. Self-esteem

Low self-esteem is related to both the aetiology and symptomatology of MDD. The DSM-5 specifies daily feelings of 'worthlessness' as part of its MDD diagnostic criteria, the ICD-10 specifically refers to 'reduced self-esteem and self-confidence' in MDD (World Health Organization, 2010), and most psychological models propose that MDD is maintained via pervasive negative views of the self (e.g. Beck et al., 1979). The current study uses the concept of 'self-esteem' rather than the specific symptom of 'worthlessness' to allow a comparison with previous research on self-esteem variability. Items measuring self-esteem tend to be more moderately phrased than those that measure worthlessness, and thus are more likely to detect intra-day variation (Palmier-Claus et al., 2011).

Prospective studies have consistently found that low self-esteem predicts depression in clinical and non-clinical samples (Orth et al., 2008; Rieger et al., 2016; Sowislo and Orth, 2013). A proposed mechanism underlying the relationship between low self-esteem and MDD is self-esteem variability, where relative drops in daily self-esteem trigger and maintain MDD (Kernis et al., 1998). Cross-sectional work has found higher levels of day-to-day variability in self-esteem in individuals currently experiencing depression (Franck and De Raedt, 2007; Sowislo et al., 2014), while prospective studies have found that such day-to-day self-esteem variability predicts future depression (Study 2 – Butler et al., 1994; Franck and De Raedt, 2007; Kernis et al., 1998). However, the strength of the relationship between depression and self-esteem variability is unclear, as the associations found in some of these cross-sectional and prospective studies have been weak or non-significant (Study 1 - Butler et al., 1994; Sowislo et al., 2014).

Previous work on self-esteem variability in MDD has two major limitations. Firstly, a maximum of two self-esteem measures per day have been used to derive self-esteem variability (Sowislo et al., 2014; Kernis et al., 1998). ESM studies on other populations have demonstrated that self-esteem variability can occur over a much shorter time frame, from hour-to-hour (Knowles et al., 2007; Thewissen et al., 2011). No high-frequency ESM study of self-esteem has yet been conducted on an MDD sample. This is a possible reason for the weak or non-significant associations found in some studies: as self-esteem likely fluctuates at a faster rate than day-to-day, studies with low sampling rates (i.e. one or two measurements per day) may not reliably pick up variability in this symptom.

A second limitation is that previous research has focused on a single dimension of self-esteem dynamics: intra-individual variability (standard deviation) across day-to-day measures. To our knowledge, no research has yet directly investigated the extent of between-moment instability in self-esteem in MDD; rather, previous work has used day-to-day variability as a proxy for self-esteem instability. Furthermore, research has not yet explored diurnal time-trends in self-esteem in healthy or MDD populations. The current study thus aims to improve upon previous literature by (1) using a high-frequency ESM protocol and (2) studying multiple aspects of self-esteem dynamics to provide a more nuanced account of self-esteem fluctuations in MDD.

1.2.2. Suicidality

Understanding the dynamics of suicidal ideation is of public health importance. Lability in suicidality may indicate difficulties in regulating intrusive suicidal thoughts (indicating suicide risk), while determining suicidality's diurnal time-course would highlight micro-periods of increased risk for suicide. A small number of previous studies suggest that micro-level variation is a feature of suicidality. Day-to-day instability in suicidal ideation has been found to have a stronger association with previous suicide attempts than duration or intensity of ideation (Witte et al., 2005, 2006). Furthermore, suicidal behavior has been found to follow a diurnal course: research on Italian suicide statistics, where time of death is routinely reported, has found that most suicides take place in the morning-time (Preti and Miotto, 2001; Williams and Tansella, 1987).

Little evidence exists on the intra-day dynamics of subjective suicidality. Two studies have investigated the diurnal time-trend of subjective suicidality (Nock et al., 2009; Husky et al., 2014). Contrary to work on suicidal acts, neither found suicidality to have a significant time-trend. To our knowledge, no study has yet used ESM to explore intra-day variability or instability in suicidality.

Previous studies have been limited in their ability to detect within-day variation in suicidality due to low sampling frequencies (two signals emitted per day in Nock et al. (2009) and five in Husky et al. (2014)). They also investigated only one aspect of suicidality: active suicidal thoughts. These thoughts were found to be relatively rare (7.8% of reports in Husky et al. (2014) and an intra-individual average of 1.1 suicidal reports per week in Nock et al. (2009)). Other dimensions of suicidality may be more commonly experienced in daily life. Passive suicidality deals with vague thoughts of suicide, such as thoughts of death and feelings that life is not worth living. Having 'thoughts of death' is itself part of the DSM-5 criteria for MDD (American Psychiatric Association, 2013) and such passive suicidality is associated both with active suicidal ideation and with suicidal acts themselves (Steer et al., 1993). A high-frequency intra-day measure of passive suicidal thoughts may therefore allow for a more nuanced measurement of suicidality in MDD.

1.2.3. Tiredness dynamics

Tiredness is the most prevalent symptom of MDD, with 78% of patients reporting at least moderate daily levels (Vaccarino et al., 2008). In healthy individuals, subjective tiredness has a distinctive diurnal time-trend: a V-shape pattern, where levels decline from morning to mid-day (where they reach a trough), and then rise steadily until reaching a peak in the late evening time (Dockray et al., 2010; Stone et al., 1996, 2006). However, no study has yet investigated the diurnal dynamics of tiredness in MDD. Given that the diurnal pattern in tiredness appears to be an integral part of healthy experience, understanding how the pattern differs in MDD may provide a new insight into the nature of this central symptom.

1.3. The present study

Little work has investigated the intra-day dynamics of MDD symptoms other than affect. Furthermore, work on affect dynamics has largely focused on instability and variability, neglecting the importance of diurnal time-trends in experience. In this study we aimed to extend prior work by providing a fine-grained ESM account of the within-day time-trends, instability, and variability of affect, self-esteem, passive suicidality, and tiredness in MDD. We examined multiple facets of the intra-day dynamics of affective, cognitive, and somatic symptoms in tandem in order to improve our overall understanding of the daily experience of MDD by providing (1) a phenomenological insight into how symptoms are experienced across the day in MDD and (2) an understanding of the differences between psychologically 'healthy' and 'unhealthy' patterns of experience, and as such potential targets for treatment.

Given the lack of previous research, much of this study is exploratory. For example, we had no specific hypotheses in relation to self-esteem time-trends or tiredness dynamics in MDD. Nevertheless, based on the evidence that has been discussed, we hypothesized the following:

(1) NA, self-esteem, and passive suicidality would exhibit significantly higher levels of variability and instability in MDD.

(2) Affect and passive suicidality would exhibit significantly more pronounced 'morning-worse' diurnal time-trends in MDD.

2. Method

2.1. Participants

Participants with MDD were recruited via psychiatric treatment centers across Dublin, Ireland.[2] Individuals attending these centers were invited to partake if they were currently experiencing an MDD episode (as per DSM criteria). Control participants were recruited through an advertisement placed in a national newspaper.[3] Controls were screened via telephone interviews and were not permitted to partake if they had any psychiatric history. The age range of participants was 18–70 years. Outpatients and control participants received reimbursement for travel expenses; there was no other monetary compensation for participation. Ethical approval was granted from the relevant ethical review boards.

Participants provided informed consent and then underwent a one-to-one briefing session with a trained researcher. This involved detailed instructions on completing the ESM protocol. Participants also completed the diagnostic Mini International Neuropsychiatric Interview (MINI Plus 5.0.0, Sheehan et al., 1998), Hamilton Depression Inventory (Ham-D, Hamilton, 1960), Beck Depression Inventory (BDI, Beck et al., 1961), Rosenberg Self-Esteem Scale (RSE, Rosenberg, 1965), Beck Scale for Suicidal Ideation (BSS; Beck et al., 1988), a demographic questionnaire, and other relevant psychometric assessments (see appendices, which can be viewed online as supplemental material). Case-consensus conferences with a consultant research psychiatrist and chart reviews were conducted to verify diagnoses.

2.2. Experience sampling procedure

Following the briefing session, participants underwent 6 consecutive days of the ESM. A signal-contingent design was employed, with a sampling rate of 10 signals per day. This signal frequency allowed a fine-grained analysis of diurnal symptom rhythms and fluctuations between moments, while the spacing of signals captured experiences that spanned the day – morning, afternoon, and evening.

On each ESM day, participants were instructed to go about their daily activities as normal, while wearing a pre-programmed wristwatch between the hours of approximately 8 a.m. and 10:30 p.m. During each of ten 90-min intervals over the day, the wristwatch paged participants. On hearing the pager, participants were instructed to complete a 2–5 min questionnaire on their immediate symptom levels. On the day following the ESM period, participants underwent a de-briefing session where they returned their completed ESM materials, which were checked for validity and rates of completion.

A pen-and-paper ESM was used to facilitate ease of use and open-ended answers (results of the latter are not included here). With pen-and-paper ESM modes, there is a risk that surveys could be completed at a later time and therefore measure retrospective rather than momentary feelings (Stone et al., 2002). To reduce the likelihood of this, the signal-contingent pen-and-paper method asks participants to record the current time (as per their ESM wristwatch) at the end of each momentary report. As the time at which participants were paged or 'beeped' varied across hours and days, it was improbable that participants could guess correctly at a later stage the time at which each beep occurred. Therefore, responses were validated by matching the self-reported time of completion of each survey with the pre-programmed time of each beep. The semi-random design of the signal-contingent ESM paper mode has been shown to be as valid as computerized versions (Green et al., 2006; Houben et al., 2015; Palmier-Claus et al., 2011).

2548 momentary surveys were collected. In line with previous ESM studies on MDD and suicidal samples, responses given outside of 25 min from the time of the signal were excluded from analysis (Peeters et al., 2006; Husky et al., 2014). Participants who did not provide enough data to ascertain diurnal trends (at least 30% of reports per day over at least 2 days) were excluded from the data. These exclusion criteria resulted in a loss of 313 reports (117 control and 196 MDD reports) and two individuals (MDD participants) with less than the recommended number of reports. The remaining sample consisted of 2231 episodes: 1205 control episodes and 1026 MDD episodes.

2.3. ESM measures

The ESM questionnaire was designed to capture key clinical dimensions of daily experience in MDD. Each item was measured via a Likert scale, ranging from 1 (not at all) to 7 (very). Multilevel exploratory factor analysis with oblique rotation was conducted using Mplus (version 8). This suggested that the ESM items were measuring distinctive symptom constructs.

2.3.1. Affect

Items from previous research were used to measure affect (Peeters et al., 2006; Stone et al., 2006). Individuals were asked to rate their current levels of '*happy*', '*relaxed*', '*interested*', and '*enjoying myself*' (PA items) and '*irritated*', '*down*', '*anxious*', '*tense*', '*ashamed,*' and '*guilty*' (NA items). Multilevel exploratory factor analysis with oblique rotation on raw affect scores yielded a two-factor solution according to the Kaiser criterion (Eigenvalue > 1) at both the between and the within-person levels. PA item loadings on Factor 1 (PA factor) ranged from 0.78 to 0.99 at the between-person level and 0.43–0.82 at the within-person level. NA item loadings on Factor 2 (NA factor) ranged from 0.74 to 0.95 at the between-person level and 0.30–0.91 at the within-person level. NA items were averaged to form an ESM NA score (between-person composite reliability = 0.84; within-person composite reliability = 0.50), while PA items were averaged to form an ESM PA score (between-person composite reliability = 0.82; within-person composite reliability = 0.46). 80.3% / 44.4% of the total between/within-person variance in the PA items was explained by the PA factor, and 82.9% / 39.5% of the between/within-person variance in NA items was explained by the NA factor. In line with previous literature, PA and NA scores appeared to measure separate constructs (Watson and Clark, 1997). Correlations between PA and NA scores were moderate: $r = 0.51$, $p < 0.001$ for MDD participants, $r = 0.59$, $p < 0.001$ for controls.

2.3.2. Self-esteem

Items by Thewissen et al. (2011) were used to measure self-esteem in daily-life: '*I like myself*', '*I am a good person*', '*I feel useless*' (reverse-scored), and '*I am a failure*' (reverse-scored). Multilevel exploratory factor analysis with oblique rotation conducted on raw scores of these items identified one factor with an Eigenvalue > 1. This factor accounted for 71.4% of between-person variance and 31.6% of within-person variance. The four items had strong loadings (between-person loadings were 0.82–0.99 and within-person loadings 0.35–0.72). These items were summed to create the ESM self-esteem measure, with good reliability (between-person composite reliability = 0.78, within-person composite reliability = 0.44). Intra-individual means in this ESM self-esteem item correlated strongly ($r = 0.87$, $p < 0.001$) with the RSE, a well-established 10-item scale of global self-esteem level (Rosenberg, 1965).

2.3.3. Suicidality

ESM research has found an aversion effect to extreme or negatively

[2] The centers involved in this research were St. John of God's Psychiatric Hospitaller Services, St. Patrick's University Psychiatric Hospital, St. Vincent's University Hospital and Glenmalure Community Day Centre in Dublin, Ireland.

[3] *Irish Times Health Supplement*, 2013, February 26th, p. 8.

Table 1
Total between-person variance (Var u_k), differences between MDD and control within-person variance [Var ($e_{ik}^{MDD} - e_{ik}^{C}$)], and Intraclass Correlation Coefficients (ICCs) for ESM symptom measures for the total sample and for MDD and control groups separately.

Symptom	Var u_k [95% CI]	Var ($e_{ik}^{MDD} - e_{ik}^{C}$) [95% CI]	ICC Total	ICC MDD	ICC Control
Negative Affect	1.15 [0.96, 1.38]	0.45 [0.39, 0.53]	0.75	0.66	0.53
Positive Affect	1.09 [0.91, 1.30]	0.17 [0.10, 0.29]	0.62	0.50	0.52
Self-Esteem	1.27 [1.06, 1.52]	0.22 [0.19, 0.25]	0.88	0.84	0.63
Suicidality	0.81 [0.68, 0.97]	0.16 [0.13, 0.19]	0.75	0.69	0.50
Tiredness	1.30 [1.09, 1.56]	−0.39 [−0.23, −0.68]	0.49	0.45	0.39

valenced items, including those directly assessing active suicidality (Husky et al., 2014; Nock et al., 2009; Palmier-Claus et al., 2011). With the aim of obtaining a more nuanced measure of within-day suicidality, momentary passive suicidality was assessed via the averaged sum of the more moderately worded items '*I feel that life is worth living right now*' (reverse scored) and '*I am having thoughts about death right now*'. These were adapted from similar items in the BSS, a well validated 19-item self-report of current suicidal ideation (Beck et al., 1988). Participant mean levels of the ESM passive suicidality item correlated very well with BSS scores ($r = 0.63$, $p < 0.001$) and the BDI suicide item ($r = 0.63$, $p < 0.001$). This measure was thus designed so as to detect more variation than extremely negatively valenced items. This strategy was moderately successful: 85% of MDD reports and 37% of control reports reported at least some level of passive suicidality (scoring > 1). Alongside this measure, participants were asked the more negatively valenced *'Since the last beep, have you had thoughts about physically harming yourself in any way?'* to measure directly active suicidal and self-harm ideation. As expected, this item was endorsed relatively infrequently: 3% of all MDD reports answered yes to this question (33 reports in total, nested in 12 individuals), while no control reports endorsed this item.

2.3.4. Tiredness

In line with previous literature (Stone et al., 2006), tiredness was seen to be a factor independent of cognitive-affective items, and was considered as a single item *'I feel tired'*.

2.4. Statistical analysis

As the data had a hierarchical structure, multilevel random-effects modeling was employed. Independence of data points was not assumed at the beep or day level, and within- and between-person effects were estimated simultaneously. Models for each analysis are presented beside their corresponding results. All effects were modeled as random effects (where intercepts and slopes are allowed to vary) using the "MIXED" command in *STATA/SE* version 13 (StataCorp). The residual-error structure used in all models (aside from variability models) was unstructured covariance, which estimates all associations between error terms. Robust standard errors were not used in regression analysis, due to issues with using these on small-moderate samples (Imbens and Kolesar, 2016). In these models, *MDD* = group status (a binary variable where 1 = MDD group and 0 = control group); i = ESM report/beep level; j = day level; and k = individual level. β is the fixed regression coefficient.

3. Results

3.1. Participant characteristics

MDD participants completed an average of 33.1 valid ESM questionnaires per individual, compared to an average of 36.5 for controls. The difference between these was non-significant, $t(62) = 1.03$, $p = 0.31$. There were no significant differences between MDD and control groups on most demographic characteristics (see appendix A; appendices are available to view as online supplemental material). The exception was gender: there were significantly more females in the control group. All analyses therefore adjust for gender.

In terms of the MDD group, average scores on the BDI (23) and Ham-D (18.3) indicated a moderate-severe sample (see Appendix B). The MDD sample consisted mostly of inpatients (77%; see Appendix C). However, most inpatients had at least two days leave from hospital during their ESM week (97%), allowing for a comparison with outpatient participants. Thirty-three percent of the MDD sample had attempted suicide at least once in the past, while over half (58%) reported some suicidal ideation. The majority of the MDD participants (89%) had recurrent depression and 30% had a secondary diagnosis of an anxiety disorder. Ninety percent of the MDD sample were on anti-depressant medication: 12 individuals were prescribed serotonin-norepinephrine reuptake inhibiters (SNRIs), 10 were prescribed selective serotonin reuptake inhibiters (SSRIs), 3 were prescribed trycyclics (TCAs) and 3 atypical antidepressants (e.g. mirtazapine).

3.2. Symptom variability

3.2.1. Between- and within-person variance

Intercept only random-effects models were fitted for each symptom individually to establish the symptom variance accounted for by between- and within-person levels. Table 1 presents the intraclass correlation coefficients (ICCs) for each symptom (for example, the ICC for NA in the total sample is 0.75, meaning that 75% of the variance is at the between-person level and 25% is at the within-person level; for the MDD group alone the ICC is 0.66 and for the control group alone the ICC is 0.53). As shown in Table 1, all ESM symptom measures exhibited significant between-person variance (Var u_k), suggesting significant variability in all symptoms across the full sample of participants. This provides evidence against floor and ceiling effects.

3.2.2. Variability

Next, within-person variances for control [var (e_{ik}^{C})] and MDD [var (e_{ik}^{MDD})] groups were estimated to establish if these differed significantly. Random effects models with heteroskedastic errors were fitted for each symptom (Gutierrez, 2008).[4] The intercepts in these models were fixed so that the only random effect at level 1 was group (control or MDD). This model is articulated as follows:

$$Symptom_{ik} = \beta_0 + \beta_1 MDD_k + \beta_2 Age_k + \beta_3 Female_k + e_{ik}$$

$$Where: e_{ik} = e_{ik}^{C}(1 - MDD_k) + e_{ik}^{MDD} MDD_k$$

The significance of the difference between control and MDD within-person variances [var ($e_{ik}^{MDD} - e_{ik}^{C}$)] was thus established. As shown in Table 1, all five symptoms had significantly different variances between-groups. The MDD group had significantly higher variances in all symptoms with the exception of tiredness, where the control group had higher variability (displayed in Fig. 1, row a).

[4] More information on this model (including STATA commands) can be found at the following UCLA Statistical Consulting Group webpage: https://stats.idre.ucla.edu/stata/faq/how-can-i-fit-a-random-intercept-or-mixed-effects-model-with-heteroskedastic-errors-in-stata/.

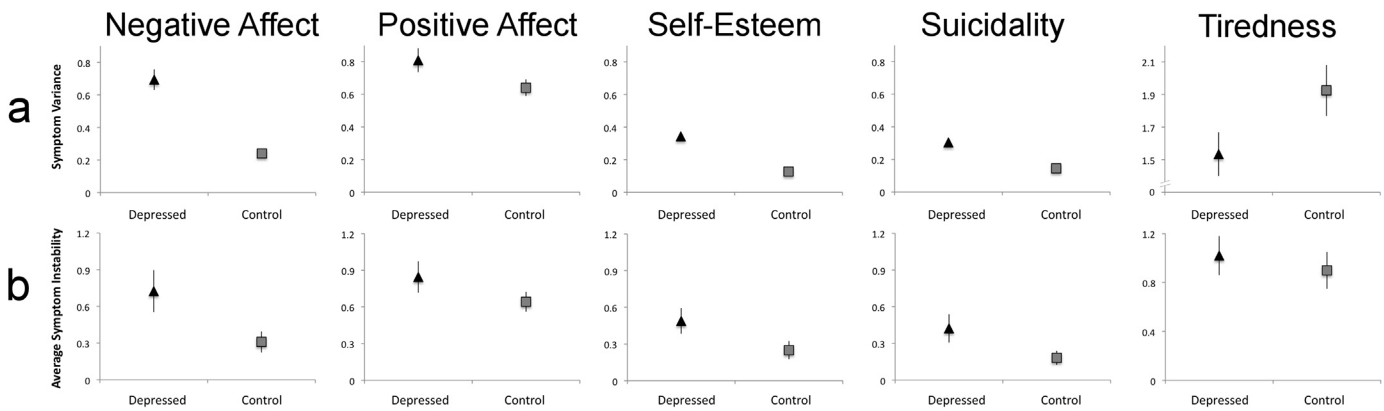

Fig. 1. Symptom variability (variances; row a) and instability (average symptom fluctuations between moments, the squared root of the successive squared difference between reports; row b) for MDD and control participants. Error bars are 95% confidence intervals.

3.3. Symptom instability

To establish symptom instability, successive squared differences between moments were calculated. These were calculated only on moments within days; the differences between evening-morning symptom levels were not included in the analysis. Successive squared difference values were then square root transformed, so that they reflected the size of the absolute change or successive difference ($|D|$) in symptom levels between measurement occasions. A two-step regression analysis was conducted to establish group differences in instability.

Step 1. In this step, MDD group was entered as the predictor variable with gender and age as controls.

$$Symptom\ |D|_{ik} = \beta_0 + \beta_1 MDD_k + \beta_2 Female_k + \beta_3 Age_k + e_{ik}$$

Average between-moment symptom fluctuations for MDD and control participants are displayed in Fig. 1, row b. Estimates from the multilevel instability analyses are displayed in Table 2. Results from step 1 were largely as predicted. Significantly higher instability was found in MDD participants in all symptoms, with the exception of tiredness where there was no significant difference between groups. NA instability showed the greatest difference between groups, with fluctuations between moments being almost half a point higher in the MDD group ($B = 0.476$; $SE = 0.074$; $p < 0.001$). PA, self-esteem and suicidality all showed between-moment fluctuations that were on average 0.27 – 0.28 points higher in the MDD group ($p < 0.001$ in each case).

Table 2
Association between MDD group status and symptom instability before (step 1) and after (step 2) adjustment for intra-individual mean symptom levels.

Symptom	B	SE	p
Step 1			
Negative Affect |D|			
MDD	0.476***	0.074	< 0.001
Positive Affect |D|			
MDD	0.276***	0.060	< 0.001
Self-Esteem |D|			
MDD	0.279***	0.058	< 0.001
Suicidality |D|			
MDD	0.272***	0.058	< 0.001
Tiredness |D|			
MDD	0.100	0.112	0.371
Step 2[a]			
Negative Affect |D|			
MDD	0.198**	0.084	0.018
Positive Affect |D|			
MDD	0.119	0.078	0.128
Self-Esteem |D|			
MDD	0.172**	0.073	0.019
Suicidality |D|			
MDD	0.082	0.063	0.193
Tiredness |D|			
MDD	−0.033	0.137	0.810

All models adjust for age and gender. $|D|$ = Successive difference score between reports. MDD = binary variable where 1 = MDD and 0 = control group.
[a] Includes control for intra-individual mean symptom level.
** $p < 0.02$.
*** $p < 0.001$.

Step 2. In the second step the intra-individual mean of the predictor symptom was entered as a covariate in the model, as some have argued that it is important to distinguish symptom instability from overall severity (Ebner-Priemer et al., 2009):

$$Symptom\ |D|_{ik} = \beta_0 + \beta_1 MDD_k + \beta_2 MeanLevel_k + \beta_3 Female_k + \beta_4 Age_k + e_{ik}$$

PA and suicidality instability no longer displayed significant associations with MDD in this step ($p > 0.05$; see Table 2). Thus, it appears that the relationship between instability in these symptoms and MDD was explained by symptom level. Both NA and self-esteem instability retained significant associations with MDD when controlling for mean symptom levels (for NA: $B = 0.198$; $SE = 0.084$; $p < 0.02$; for self-esteem: $B = 0.172$; $SE = 0.073$; $p < 0.02$).

3.4. Diurnal time-trends in symptoms

3.4.1. Modeling time-trends

As quadratic relations have been identified in numerous studies on the diurnal time-trends of affect in MDD and tiredness in the general population (e.g. Peeters et al., 2006; Stone et al., 2006), a two-step approach was used whereby the quadratic term was first tested. We therefore test whether modeling non-linear trends produces a better fit to the study data (indicated by a statistically significant quadratic term) before modeling a linear relationship. Between-group differences in diurnal trends were investigated by fitting interaction terms between MDD and the linear (*MDD*Time*) and quadratic time term (*MDD*Time²*). Time-trend effects were then modeled for each group separately using the below models. Time of day (*Time*) was treated as a continuous variable in these time-trend models.

$$Symptom_{ijk} = \beta_0 + \beta_1 Time_{ijk} + \beta_2 Time^2_{ijk} + \beta_3 Female_k + \beta_4 Age_k + e_{ijk}$$

Where no evidence for a quadratic trend was identified, a linear term was tested.

$$Symptom_{ijk} = \beta_0 + \beta_1 Time_{ijk} + \beta_2 Female_k + \beta_3 Age_k + e_{ijk}$$

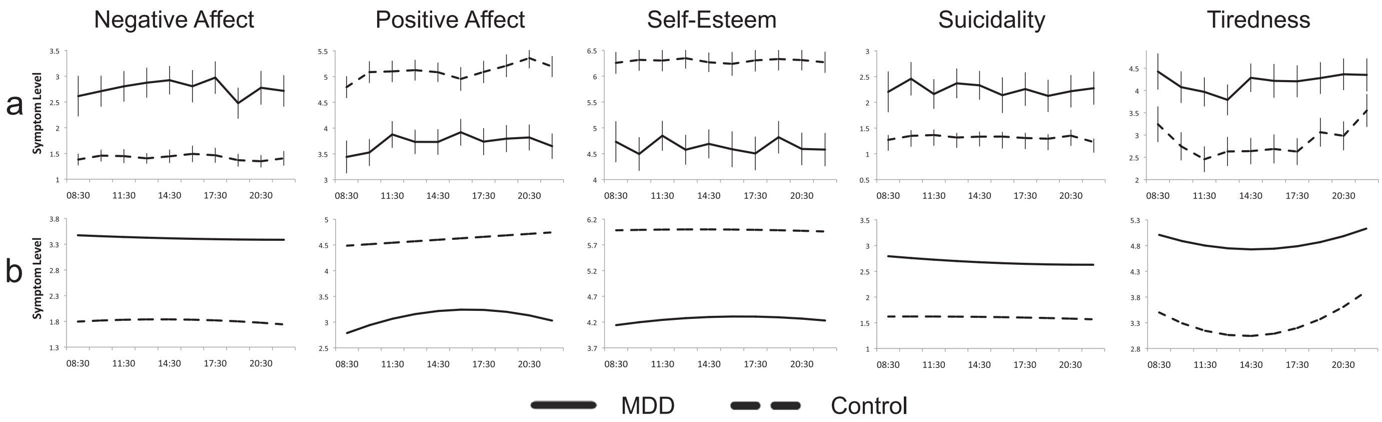

Fig. 2. Diurnal symptom patterns for MDD and control groups. Row (a) is average raw symptom scores for each time of day for each group. Error bars are 95% confidence intervals. Row (b) depicts symptom time-trends (regression lines) for control and MDD groups. Y-axis is ESM symptom level (on a Likert scale from 1 to 7). X-axis is time of day (from 8:30 a.m. to 10:00 p.m.), where each time of day refers to the mid-point of each 90-min ESM 'beep' block (each participant was beeped once during each block).

3.4.2. Results

Fig. 2 depicts the diurnal time-trends identified in each group, while Tables 3 and 4 summarize the findings in relation to these time-trend regressions. The interaction terms for NA did not reach significance ($p > 0.10$), indicating there were no statistically significant differences between-groups in this diurnal trend. As shown in Table 4, NA did not display a significant time-trend in either the MDD or control group. PA and tiredness both showed significant between-group differences in their diurnal time-trends. In PA, there were significant linear ($B = 0.175$; $SE = 0.054$; $p = 0.001$) and quadratic ($B = -0.016$; $SE = 0.005$; $p = 0.001$) interaction terms, indicating significant differences between-groups. As shown in Fig. 2, the control group displayed a linear pattern in PA, which continued to rise from morning through to late evening. The MDD group displayed an inverted-U (quadratic) PA time-trend, which rose from morning into the afternoon, before dipping slightly later in the evening.

Tiredness also displayed significantly different patterns of change between groups, indicated by the significance of the quadratic interaction term ($B = -0.015$; $SE = 0.007$; $p < 0.05$). Although the normative V-shaped quadratic pattern was identified in both MDD and control groups, the V-shape was significantly more pronounced in the control group. As seen in Fig. 2, tiredness in MDD had a much flatter shape over the day.

The linear interaction term for passive suicidality ($B = -0.012$; $SE = 0.007$; $p < 0.10$) and the quadratic interaction term for self-esteem ($B = -0.004$; $SE = 0.003$; $p < 0.10$) were of trend-level significance, suggesting somewhat different diurnal patterns of change across groups. As shown in Table 4, group-specific time-trend analyses revealed a significant and negative linear time-trend in suicidality in the MDD group ($B = -0.018$; $SE = 0.006$; $p < 0.005$), but not in the control group ($B = -0.006$; $SE = 0.004$; $p = 0.089$), while there was a significant quadratic trend in self-esteem in MDD ($B = -0.006$; $SE = 0.002$; $p = 0.017$), but non-significant quadratic and linear trends in the control group. Thus, as shown in Fig. 2, there was evidence to suggest a subtle morning peak in passive suicidality levels and inverted-U diurnal trend in self-esteem in the MDD group.

Table 3
Multilevel estimates of interaction effects between MDD group status (MDD) and linear and quadratic time of day trends.

Symptom	*B*	*SE*	*p*
Negative Affect			
Time*MDD	−0.003	0.010	0.765
Time²*MDD	–	–	–
Positive Affect			
Time*MDD	0.175**	0.054	0.001
Time²*MDD	−0.016**	0.005	0.001
Self-Esteem			
Time*MDD	0.062*	0.031	0.045
Time²*MDD	−0.004†	0.003	0.095
Tiredness			
Time*MDD	0.134	0.084	0.110
Time²*MDD	−0.015*	0.007	0.039
Suicidality			
Time*MDD	−0.012†	0.007	0.078
Time²*MDD	–	–	–

A quadratic model (Time²) was firstly tested. Where no evidence for a quadratic model was identified a linear model (Time) was tested. Models adjust for gender and age. Symptoms are measured on a Likert scale from 1 (not at all) to 7 (very). Time is measured in hours and is treated as a continuous variable.
* $p < 0.05$.
** $p < 0.01$.
† $p < 0.10$.

Table 4
Multilevel estimates of linear and quadratic time of day effects on symptoms in MDD and healthy control groups.

Symptom	MDD			Healthy Control		
	B	*SE*	*p*	*B*	*SE*	*P*
Negative Affect						
Time	−0.009	0.009	0.292	−0.006	0.005	0.175
Time²	–	–	–	–	–	–
Positive Affect						
Time	0.203***	0.046	< 0.001	0.028	0.007	< 0.001
Time²	−0.016***	0.004	< 0.001	–	–	–
Self-Esteem						
Time	0.075**	0.029	0.009	−0.003	0.003	0.440
Time²	−0.006*	0.002	0.017	–	–	–
Tiredness						
Time	−0.172**	0.061	0.005	−0.304***	0.057	< 0.001
Time²	0.017***	0.005	0.001	0.032***	0.005	< 0.001
Suicidality						
Time	−0.018**	0.006	0.003	−0.006	0.004	0.089
Time²	–	–	–	–	–	–

A quadratic model (Time²) was firstly tested. Where no evidence for a quadratic model was identified a linear model (Time) was tested. Models adjust for gender and age. Symptoms are measured on a Likert scale from 1 (not at all) to 7 (very). Time is treated as a continuous variable.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

4. Discussion

All five symptom constructs displayed distinct intra-day profiles in MDD when compared to those of healthy controls. Cognitive-affective symptoms exhibited significantly *increased* variation in the daily life of individuals with MDD. In contrast, the one somatic symptom studied, tiredness, exhibited significantly *decreased* within-day variation in MDD. This indicates that as well as the overall severity of symptoms, symptom dynamics also define the daily experience of MDD and separate it from healthy psychological experience.

4.1. Increased variability and instability in cognitive and affective symptoms

Negative affect (NA), positive affect (PA), self-esteem, and passive suicidality all exhibited large and frequent within-day fluctuations in the MDD group. In line with a large body of previous work (Houben et al., 2015), NA showed the greatest difference between groups in instability and variability. Unlike most previous studies, however, increased instability and variability were also found in PA in MDD (albeit to a lesser extent than NA). This supports arguments for the importance of PA dynamics in depression (Gruber et al., 2013). MDD was also strongly associated with self-esteem variability and instability. This is in keeping with earlier work on self-esteem variability in MDD (Franck and De Raedt, 2007) and argues against more recent work positing that self-esteem variability is not a significant aspect of MDD (Sowislo et al., 2014). Increased variability and instability in passive suicidality was another feature of MDD symptom dynamics. Previous work has shown an association between increased day-to-day instability in suicidality and past suicide attempts (Witte et al., 2005, 2006). Lability in suicidal thoughts may therefore prove to be an important factor in understanding suicide risk.

The relationship between MDD and symptom instability differed somewhat across cognitive-affective symptoms. Instability in NA and self-esteem had strong associations with MDD that were independent of the severity (mean-levels) of these symptoms. However, mean symptom levels appeared to explain the relationship between MDD and instability in PA and suicidality: as the severity of daily passive suicidality increased, so did instability in the intensity of such thoughts, while as overall PA levels decreased, PA instability increased.

4.2. Diurnal time-trends in positive affect, tiredness, suicidality, and self-esteem

Diurnal time-trends were identified in PA, tiredness and, to some degree, passive suicidality and self-esteem. Although NA exhibited high levels of instability and variability in MDD, it did not display a significant diurnal time-trend. This was surprising, as a significant ‘morning worse’ NA trend is a feature of previous conceptualizations of diurnal mood variation in MDD (Leibenluft et al., 1992; Peeters et al., 2006). Instead, the morning-worse MDD pattern was manifest in PA.

PA in MDD displayed significantly more diurnal variation than controls: it had an inverse-U shape (compared to a linear trend in controls) with a steeper overall increase from morning lows to evening highs. This pronounced diurnal pattern found in MDD PA is at odds with the findings of Murray (2007), where depression was associated with a weakened and flatter diurnal PA pattern. Instead, our findings replicate the more pronounced quadratic MDD PA pattern found in Peeters et al. (2006). The finding that ‘morning-worse’ mood in MDD is expressed via PA lows rather than NA highs is in keeping with recent research, which also found the ‘morning-worse’ depression pattern to be much more pronounced in PA than NA (Daly et al., 2011). Again, this emphasizes the prevalence and importance of PA dynamics in MDD.

To a lesser extent, suicidality and self-esteem also displayed morning-worse patterns in MDD. In the MDD group, self-esteem displayed an inverse-U shape, but to a much lesser extent than PA. In suicidality, a significant linear trend with a morning peak was detected in the MDD group. This is similar to the morning peaks identified in previous research on suicidal acts (Preti and Miotto, 2001; Williams and Tansella, 1987). However, the findings in relation to the time-trends of self-esteem and suicidality should be interpreted with caution: as can be seen in Fig. 2, both trends were very subtle, and although the trends were significant in the MDD group, neither were found to be significantly different from those of control participants.

Tiredness was uniquely defined by *decreased* diurnal dynamics in MDD. The control group had higher variances, a more pronounced V-shaped diurnal pattern, and a steeper overall increase from morning to evening levels than the MDD group. Relative to controls, individuals with MDD experienced tiredness at a high and constant level during the day, with less of a mid-day nadir in levels. It appears that individuals with MDD do not feel relatively more tired at night compared to the rest of their day. This diurnal pattern could help to explain the apparently paradoxical MDD experience of low levels of daily energy and motivation, yet difficulties in getting to sleep in the evening time.

4.3. Theoretical differences between variability, instability, and diurnal time-trends

It is important to briefly consider the theoretical differences and relationships between the dynamics measured, and what they can tell us about the nature of the symptoms studied. Variability refers to how much symptoms deviate from average levels over the course of the day. Variability can be expressed in a number of ways: gradual changes in symptom levels throughout the day, as well as large changes from one moment to the next (i.e. instability). Therefore, although the three concepts measured in this study are related (if an individual has high instability or a pronounced diurnal time-trend, he/she will also have high variation from mean levels and thus high variability), they are not the same thing.

For example, decreased variability – but not instability – was found in tiredness in the MDD group. It appears that the difference one feels in tiredness levels from one moment to the next is not as important as a more gradual variation in overall levels across the day. This gradual variation in tiredness was expressed as a systematic diurnal time-trend. This study emphasizes that it is important to measure multiple aspects of daily symptom dynamics. Variability tells us the extent to which symptom levels change across the day, while other aspects (instability and time-trends) give important phenomenological information on *how* this variation is experienced.

4.4. Possible mechanisms underlying symptom dynamics

This study's aim was to provide a descriptive account of the dynamics of MDD symptom constructs, not to explain why or how these symptoms fluctuate as they do across the day. Nevertheless, we tentatively suggest two possible mechanisms underlying symptom dynamics: difficulties in emotion regulation and dysregulation in biological circadian rhythms.

Common features across cognitive-affective symptoms in MDD are emotion regulation deficits and a lack of cognitive control (Joormann and Vanderlind, 2014). Such deficits result in difficulties moderating cognitive and affective reactions to both external events and internal thoughts (such as suicidal cognitions and negative self-thoughts), and could therefore lead to the frequent and amplified fluctuations found in affect, self-esteem, and suicidality.

The finding that tiredness did not show increased variability or instability in MDD suggests that this symptom is relatively unreactive to thoughts or external events. Previous work has found that, unlike other subjective experiences, diurnal variation in tiredness is not dependent on the activities in which an individual is engaged (Stone et al., 1996, 2006). Instead, tiredness dynamics may be more influenced by endogenous circadian variation in biological systems. The HPA axis plays an important role in regulating sleep-wake cycles and energy mobilization and thus influences subjective feelings of fatigue and tiredness throughout the day (Harris et al., 2015; Tops et al., 2006). A flatter slope in cortisol output has been identified in individuals with depression (Stetler and Miller, 2005). HPA axis dysregulation could therefore contribute to the similarly flatter diurnal rhythm found in MDD tiredness.

Likewise, the MDD 'morning worse' diurnal trend in affect has traditionally been thought to be due to a dysregulation of circardian rhythms in biological processes, such as HPA axis activity and melatonin secretion (Hall et al., 1964; Moffot et al., 1994). More recent research has found that morning lows in affect are linked with lower than average cortisol levels in the hours after waking (Daly et al., 2011). Experimentally administered cortisol has been found to induce feelings of energy and vigor (Plihal et al., 1996; Tops et al., 2006). Energy, alertness, and vigor are aspects of the construct of PA (Watson and Clark, 1997). Therefore, it makes sense that the affective correlates of low morning cortisol levels would be expressed via a lack of PA rather than intense NA – and thus a morning-worse pattern in PA, rather than NA. Uncovering the mechanisms that underlie MDD symptom dynamics will be a fruitful area of future research.

4.5. Limitations

This study has a number of limitations. Firstly, the majority of the MDD sample was receiving pharmacotherapy. Including patients on medication resulted in a sample that reflects the psychiatric MDD population. Nevertheless, it may be the case that the effects of anti-depressant medication drove the group differences in symptom dynamics found in this study, rather than depression *per se.* However, research has found that imipramine reduces the variability of quality of life ESM reports in individuals with MDD (Barge-Schaapveld and Nicolson, 2002), suggesting that the differences found between groups in the current study may be even more marked in a non-medicated sample. Further research is required to establish the differential effect of anti-depressant treatment on the dynamics of different MDD symptoms.

The MDD sample also consisted of a mix of inpatient and outpatient participants. We argue that these samples are comparable, since outpatients were treated at the same facilities as inpatients during the day, were taking the same medications, and had similar levels of depression. Additionally, inpatients took at least two days' leave from their hospital stay during the ESM week.

The passive suicidality measure has not been used in ESM research previously. It is therefore unknown whether it is a good proxy for more active suicidal thoughts and behaviors. However, it correlated strongly with both BDI and BSS assessments, suggesting that it was tapping into subjective suicidality. This measure was designed to capture more variability than negatively valenced suicide items and was endorsed to a far greater extent than the question directly assessing self-harm and suicide. However, although 85% of MDD ESM reports and over a third of control reports reported at least some level of passive suicidality, controls nevertheless displayed very low scores on this measure, which may have curtailed the variability that could be identified in this group.

Likewise, the case-control design meant that the control group exhibited much lower NA and much higher self-esteem scores than the MDD group. As with suicidality, it may be the case that floor and ceiling effects reduced the ability to detect variation in these symptoms in the control group. We argue that the results found in these symptoms are still meaningful because in analyses where mean levels were controlled for (i.e. instability analysis), significant differences remained across groups. This indicates that mean levels cannot fully explain the differences found between MDD and control groups in self-esteem and NA instability. Nonetheless, a recommendation for further research is to produce more fine-grained measures of suicidality, NA and self-esteem that use more items, less negatively worded items and response scales that allow for small variations to be identified (such as visual analogue scales). Such measures may be able to detect more variablity in these symptoms. Including psychiatric as well as healthy control groups may also allow a more nuanced exploration of daily dynamics in MDD experience.

4.6. Conclusions and future directions

This study provides a systematic, multidimensional exploration of five subjectively experienced MDD symptom constructs: PA, NA, self-esteem, suicidality, and tiredness. We found evidence that the MDD group differed from the control group across all symptoms investigated, each of which showed evidence of distinct diurnal time trends and/or patterns of variability and instability in MDD. This study sets the stage for additional ESM studies to test these relationships further and explore the dynamics of an even broader range of MDD experiences and behavior. Longitudinal designs hold particular promise, as the usefulness of this intra-day dynamics approach will ultimately lie in its predictive power in forecasting diagnoses, treatment, and recovery (van de Leemput et al., 2014; Wichers et al., 2010).

Individual depression symptoms have recently been found to be associated with different risk factors, treatment responses, biomarkers and effects on psychosocial functioning (see review by Fried and Nesse, 2015). Research suggests that different within-day dynamics in affect also have differential associations with psychological functioning (Gruber et al., 2013), biological functioning (Daly et al., 2011, 2014; Peeters et al., 2003) and treatment outcomes (Wichers et al., 2012). It is likely therefore that dynamics in the other depression symptoms explored in this study – self-esteem, suicidality and tiredness – also play distinct roles in MDD outcomes. Broadening the focus of depression research to include within-day symptom dynamics (alongside symptom severity) will help us to understand and ultimately treat more effectively the daily experience of MDD.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.psychres.2018.02.032.

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