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Mood disorders in everyday life

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Published in:
Clinical Psychology Review

DOI:
10.1016/j.cpr.2012.05.007

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2012

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Aan het Rot, M., Hogenelst, K., & Schoevers, R. A. (2012). Mood disorders in everyday life: A systematic review of experience sampling and ecological momentary assessment studies. *Clinical Psychology Review*, *32*(6), 510-523. https://doi.org/10.1016/j.cpr.2012.05.007

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Clinical Psychology Review 32 (2012) 510–523

Contents lists available at SciVerse ScienceDirect

Clinical Psychology Review

Mood disorders in everyday life: A systematic review of experience sampling and ecological momentary assessment studies

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ARTICLE INFO

Article history:
Received 5 December 2011
Received in revised form 23 May 2012
Accepted 24 May 2012
Available online 6 June 2012

Keywords:
Everyday life
Mood
Major depressive disorder
Bipolar disorder
Event-contingent recording
Within-person variation

ABSTRACT

In the past two decades, the study of mood disorder patients using experience sampling methods (ESM) and ecological momentary assessment (EMA) has yielded important findings. In patients with major depressive disorder (MDD), the dynamics of their everyday mood have been associated with various aspects of their lives. To some degree similar studies have been conducted in patients with bipolar disorder (BD). In this paper we present the results of a systematic review of all ESM/EMA studies in MDD and BD to date. We focus not only on the correlates of patients' everyday mood but also on the impact on treatment, residual symptoms in remitted patients, on findings in pediatric populations, on MDD/BD specificity, and on links with neuroscience. After reviewing these six topics, we highlight the benefits of ESM/EMA for researchers, clinicians, and patients, and offer suggestions for future studies.

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Contents

1. Introduction . . . 511
2. Methods . . . 512
3. Results . . . 512
   3.1. Overview of the selected studies . . . 512
   3.2. Topic 1: contextual factors and abnormal internal affective states in major depressive disorder . . . 512
   3.3. Topic 2: effects of treatment . . . 514
   3.4. Topic 3: residual symptoms in remitted patients . . . 515
   3.5. Topic 4: findings specific to pediatric populations . . . 515
   3.6. Topic 5: findings specific to bipolar disorder . . . 516
   3.7. Topic 6: the neuroscience of mood disorder patients' everyday lives . . . 517
4. Discussion . . . 518
   4.1. General summary . . . 518
   4.2. Rationale for using ESM/EMA for the study of mood disorders . . . 518
   4.3. Limitations at the level of ESM/EMA data collection, analysis, and interpretation . . . 519
   4.4. Opportunities for the future . . . 520
   4.5. Summary and conclusion . . . 521
5. Declaration of interest . . . 521
Acknowledgment . . . 521
References . . . 521

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doi:10.1016/j.cpr.2012.05.007

1. Introduction

In clinical practice symptoms are usually assessed retrospectively. It has been argued, however, that mood disorder patients' symptom recall is biased by their dysfunctional attitudes about themselves and their surroundings. This may lead them to selectively attend to negative aspects of their everyday lives (Beck, 1963). A study by Mokros (1993) highlights the effect this recall bias might have in clinical practice. Seven adolescents were diagnosed with a major depressive episode by an experienced clinician. A week later all patients were still considered depressed, based on the clinician's ratings of their recalled symptoms. Crucially, however, this finding was not in agreement with patients' real-time reporting of these symptoms. During the week patients had repeatedly completed short, standardized forms in response to frequent, irregularly occurring pager signals. There were clear discrepancies between patients' reporting of symptoms during the week and their recall of these symptoms at the end of the week.

In psychology, the method used by Mokros (1993) to repeatedly assess people in real-time is best known as experience sampling (Larson & Csikszentmihalyi, 1983). Experience sampling aims to systematically obtain self-report data on participants' everyday lives at many points in time. To this end participants are generally required to carry pagers signaling at unpredictable intervals, usually in the range of 1–2 h, and to complete forms as soon as possible after each pager signal. This is known as signal-contingent data recording. With up to 10 signals per day over multiple days, and usually only a few missed signals, the number of repeated measurements per participant is much higher than the number obtained with more traditional self-report measures. Experience sampling has been extensively validated (Csikszentmihalyi & Larson, 1987).

In medicine, experience sampling is probably better known as ecological momentary assessment (Stone & Shiffman, 1994). While the term was coined less than two decades ago, ecological momentary assessment has its roots in the development of clinical research diaries in the 1940s, ecological studies of behavior in the 1960s and 1970s, and ambulatory devices for continuous monitoring of cardiovascular activity in the 1980s (for a review see Shiffman, Stone, & Hufford, 2008). Traditionally there were some differences between experience sampling and ecological momentary assessment. Experience sampling was designed to measure people's internal affective states and associated activities at random time points during the day and so data recording has generally been signal-contingent. Ecological momentary assessment has focused more on actual behaviors and has been more likely to include the concurrent measurement of physiological variables such as blood pressure (Kamarck et al., 2002). Additionally, data recording has been more likely to be event-contingent, i.e. participants provide data right after the occurrence of certain events of interest, which may vary depending on the research question. Notably, events of interest may be more likely to occur in some people than in others, and their frequency may also change from day to day within individual persons. For example, when studying affect in relation to cigarette smoking, participants would be asked to record data every time they smoke (Shiffman, 2009).[1] In spite of these historical differences between 'experience sampling methods' (ESM) and 'ecological momentary assessment' (EMA), the two terms are increasingly used together (Stone & Shiffman, 2002; Trull & Ebner-Priemer, 2009; Wenze & Miller, 2010). We will do the same.

Given the focus on people's internal affective states, activities, and behaviors, it is not surprising that ESM/EMA is increasingly used in mood disorders research. Ebner-Priemer and Trull (2009) reviewed relevant studies in adults with major depressive disorder (MDD), bipolar disorder (BD), or borderline personality disorder. They focused their discussion on data supporting the advantages of ESM/EMA: mood is assessed in real-time, repeatedly, and in everyday life situations. This way recall bias can be avoided, the dynamics of mood can be revealed, and the data can be easily generalized. Mood can be assessed in specific contexts and over the course of treatment so the factors that alter mood can be elucidated and treatment progress can be studied closely. Also, mood can be assessed together with actual behavior as well as with physiological variables. Ebner-Priemer and Trull (2009) did not include studies in pediatric populations in their review. This is unfortunate because studying the everyday lives of youth with mood disorders is valuable given age-related differences in the clinical presentation of these disorders (e.g., Kovacs, 1996; Leibenluft, Blair, Charney, & Pine, 2003). It is conceivable that mood may be influenced by, and may influence, other aspects of everyday life in children and adolescents than in adults. One of the benefits of ESM/EMA is that the variables under study may be changed to suit the population of interest.

Another review on the use of ESM/EMA in mood disorders research did include studies in pediatric populations (Wenze & Miller, 2010). Like Ebner-Priemer and Trull (2009), the authors reviewed the types of questions relevant to mood disorders that ESM/EMA is especially suitable to answer. Moreover, they discussed the feasibility of using ESM/EMA in patients with MDD or BD and compared the different kinds of data-collection formats used to date (i.e. paper forms versus hand-held computers versus investigator-administered phone interviews). Together, these reviews provide valuable insight into the opportunities ESM/EMA offers to mood disorder researchers and form important additions to reviews focusing on the pros and cons of ESM/EMA in general (e.g., Moskowitz, Russell, Sadikaj, & Sutton, 2009; Shiffman et al., 2008). However, one limitation of these reviews is that they mostly focus on the methods of the selected studies and are therefore more relevant to researchers than to clinicians. A systematic review of the specific results and practical applicability of relevant ESM/EMA studies will be useful for both researchers and clinicians interested in the everyday dynamics of mood disorder symptoms.

Providing this review now seems especially timely for multiple reasons. Firstly, it has been 20 years since the publication of deVries' (1992) book on the use of ESM/EMA in clinical populations. deVries has since been involved in multiple relevant studies in MDD and BD. Over the years ESM/EMA has become much more sophisticated, especially in its data analytic approaches, with promising potential for both research and clinical practice. Secondly, and in line with these rapid developments, there has been a notable boost in the number of publications on ESM/EMA in mood disorder patients. Many of the currently available data have been published in the past few years and have not previously been reviewed. Thus, we feel it is time for a systematic review of the insights gained from ESM/EMA studies in mood disorder patients.

Specifically, and in line with our interest in the clinical insights that are emerging from this growing body of literature, we structure this review using six main topics. Firstly, we focus on the dynamics of mood in symptomatic MDD patients, in other words what contextual factors are associated with patients' affective states? This may provide insight in the potential causes of MDD symptoms and perhaps contribute to the future development of new forms of (more personalized) treatment. Secondly, we focus on the impact of existing forms of treatment on MDD patients' internal affective states,

[1] We are aware that the occurrence of certain events of interest can be recorded using either an event-contingent data recording approach or a signal-contingent data recording approach. However, when a signal-contingent data recording approach is used, it is only possible to inquire about 'recent' events (e.g. Myin-Germeys et al., 2003; Peeters et al., 2003b). In this case, events may occur several hours before the data recording takes place. In contrast, when an event-contingent data recording approach is used, no such lag exists. This is useful not only when studying physiological responses to specific events (e.g. Kamarck et al., 2002), but also when asking participants about details of the characteristics of these events (e.g., Moskowitz, 1994). We return to this advantage of event-contingent data recording in the Discussion.

activities, and behaviors. This may provide insight into how exactly depressed patients undergoing treatment improve clinically over time. Thirdly, we focus on the characterization of residual symptoms that may continue to exist in MDD patients even when clinical improvement has been obtained. Mood disorders are considered chronic illnesses and characterizing patients' residual symptoms may provide insight into why many remitted patients relapse; this might in turn contribute to the development of new relapse prevention strategies. Fourthly, we focus on pediatric populations of MDD patients. There are age-related differences in the clinical presentation of MDD (Kovacs, 1996) and ESM/EMA may provide insight in how the everyday lives of children and adolescents with MDD might influence and be influenced by their mood in ways that are unique to this age group. Fifthly, we focus on the differences from MDD and BD that have been revealed by ESM/EMA. This seems particularly relevant in the context of the publication of the fifth version of the Diagnostic and Statistical Manual of Mental Disorders (DSM) in 2013, for which specific categories for "Depressive Disorders" and "Bipolar and Related Disorders" have been proposed. Sixthly and lastly, we focus on the relatively recent inclusion of neurobiological variables (e.g. cortisol) in ESM/EMA studies of mood disorder patients. These types of studies may provide valuable insight into the neuroscience of mood disorder patients' everyday lives.

Before describing the available data for each of these six topics, we clarify the methods used to select the relevant studies and summarize the methodological characteristics of these studies. Afterwards, we briefly mention the advantages and disadvantages of using ESM/EMA for the study of mood disorder patients and then move to discussing the implications for clinical practice and providing multiple suggestions for future research.

2. Methods

In May 2012 we searched the online PsycInfo and PubMed databases for relevant studies using the following string of search terms: ("diary" OR "ecological momentary assessment" OR "experience sampling") AND ("affective disorder" OR "bipolar disorder" OR "depression" OR "mood disorder"). Like Wenze and Miller (2010), we only included studies in which participants met clinical criteria for MDD or BD, had a primary diagnosis of a mood disorder, and were assessed outside the laboratory more than once per day. If articles found using our search cited additional studies that met our criteria, then these were also included. Studies published before 1994 were excluded since they did not use the current version of the DSM (American Psychiatric Association, 1994, 2000) to diagnose the mood disorder; participants in these early studies (e.g., Mokros, 1993) suffered from major depressive episodes but it is unclear whether they had MDD or BD. Studies in inpatients residing on hospital wards were also excluded, as were outpatient studies that took place over 24 h or less. Finally, dissertations were excluded, as were studies not published in English.

3. Results

3.1. Overview of the selected studies

Table 1 provides an overview of the 48 included papers. Most studies compared patients with MDD to healthy controls, some compared patients with BD (mostly type 1) to healthy controls, and a few made direct comparisons between MDD and BD patients or between mood disorder patients and other groups of patients. Most MDD studies involved currently depressed patients. In contrast, all but two BD studies exclusively involved patients who were in remission. In about one-third of all studies, patients were not medicated at the time of inclusion (all of these patients were currently depressed), in about one-fourth at least some patients were medicated, and in the remainder medication status was not specified. A majority of studies included patients of both genders.

More than half of the papers included in our review were published after the reviews by Ebner-Priemer and Trull (2009) and Wenze and Miller (2010). Most studies used a signal-contingent data recording approach; some used a time-contingent approach (i.e. participants record data at predetermined fixed times of the day). The number of studies that used paper forms for data recording is similar to the number of studies that used personal digital assistants (PDAs). PDAs were first used for ESM/EMA studies in mood disorder patients less than a decade ago (Myin-Germeys et al., 2003). Their use has increased over time, but the paper forms remain popular. Across all papers, the average number of measurement days was 11 (range 3–54), the average number of repeated measurements per day was 7 (range 2–10), and the average total number of repeated measurements was 70 (range 12–420). Note that these numbers represent study methods, not results.

Many studies measured current levels of positive affect (PA) and negative affect (NA). PA includes internal states like interested, excited, and alert. NA includes internal states like distressed, irritable, and nervous. PA and NA have both been identified as fundamental to the dynamics of mood (Watson & Tellegen, 1985). Importantly, while PA and NA are generally considered independent when measured over time across situations (Bradburn, 1969), the debate on their independence within a given situation is still ongoing (Egloff, 1998; Feldman Barrett & Russell, 1998; Goldstein & Strube, 1994; Schmukle, Egloff, & Burns, 2002). We briefly acknowledge this debate here and will return to it when discussing limitations to our interpretations of the studies' findings.

3.2. Topic 1: contextual factors and abnormal internal affective states in major depressive disorder

Many ESM/EMA studies in symptomatic MDD patients have in some way focused on how contextual factors may influence affect, or be influenced by it, by first establishing to what extent patients report abnormal levels of PA and NA across situations, and then considering various variables that might be associated with PA and NA on a situation-by-situation basis. So far these variables have included quality of life perceptions, stress experiences, recent emotional events, sleep, and physical activity.

For example, the group of deVries has repeatedly found that on average adults with MDD report less PA and more NA than healthy controls (Barge-Schaapveld et al., 1999; Myin-Germeys et al., 2003; Peeters, Nicolson, Berkhof, Delespaul, et al., 2003). Barge-Schaapveld et al. (1999) additionally measured patients' enjoyment of their current activities, physical complaints, and perceptions of their quality of life. On average, MDD patients reported less enjoyment of everyday activities, more complaints, and a poorer quality of life, than healthy controls. More importantly, when the ESM/EMA data were analyzed in more detail (but not when a global retrospective measure was used at the end of the EMS/EMA period), it was found that patients reported their quality of life to be poor specifically in situations in which they also reported low levels of PA, high levels of NA, a lack of enjoyment of current activities, and physical complaints. Knowing which symptoms may prevent patients from reporting a good quality of life, and that it may be patients' poor perceptions of their quality of life that may lead them to report less PA and more NA, is essential because improved quality of life is considered an important outcome in the treatment of MDD (IsHak et al., 2011).

Low levels of PA and high levels of NA in MDD patients compared to controls may also be attributed to patients' relatively high levels of current stress. However, Myin-Germeys et al. (2003) found that only the association between current stress and NA levels was stronger in the patients than in the controls; the association between current stress and PA levels was equally strong in both groups. In

Table 1
Overview of papers included in the systematic review.

	Patient group			Comparison group(s)		Measurement method				
	N	Symptomatic	Medicated	N	Description	Days	Observations per day	Observations	Contingency	Format
Diagnosis MDD										
Adults										
Barge-Schaapveld et al., 1995	21	Yes	No	–	–	12	10	120	Signal	Paper
Barge-Schaapveld et al., 1999	63[a]	Yes	No	22[b]	Healthy	6	10	60	Signal	Paper
Barge-Schaapveld and Nicolson, 2002	63[a]	Yes	No	22[b]	–	21	10	210	Signal	Paper
Ben-Zeev et al., 2009	26	Yes	Unknown	25	Healthy	7	8	56	Signal	PDA
Bower et al., 2010	35[c]	Yes	Mixed	36[d]	Healthy	3	10	30	Signal	PDA
				25[e]	mDD					
Bylsma et al., 2011	35[c]	Yes	Mixed	38[d]	Healthy	3	10	30	Signal	PDA
				26[e]	mDD					
Delespaul et al., 2002	41	No	Unknown	67	PD	6	10	60	Signal	Paper
Geschwind, Nicolson, et al., 2011	63[a]	Yes	No	–	–	9	10	90	Signal	Paper
Geschwind, Peeters et al., 2011	130	Yes	Mixed	–	–	12	10	120	Signal	Paper
Husky et al., 2009	55	No	Unknown	55	Healthy	7	5	35	Signal	PDA
Husky et al., 2010	20	Unknown	Unknown	–	–	3	5	15	Signal	PDA
Jahng et al., 2008[1]	38	Yes	Unknown	46	BPD	28	6	168	Signal	PDA
Jahng et al., 2011[1]	50	Yes	Unknown	74	BPD	28	6	168	Signal	PDA
Knowles et al., 2007	16	No	Unknown	19[f]	Healthy	7	2	14	Time	Paper
Mata et al., 2012	53	Yes	Unknown	53	Healthy	7	8	56	Signal	PDA
Myin-Germeys et al., 2003	46[g]	Yes	No	49[h]	Healthy	6	10	60	Signal	Paper
				42[i]	PD					
Peeters, Nicolson, & Berkhof, 2003	45[g]	Yes	No	39[j]	Healthy	6	10	60	Signal	Paper
Peeters, Nicolson, Berkhof et al., 2003	46[g]	Yes	No	39[j]	Healthy	6	10	60	Signal	Paper
Peeters et al., 2006	47[g]	Yes	No	39[j]	Healthy	6	10	60	Signal	Paper
Peeters et al., 2010	47[g]	Yes	No	–	–	6	10	60	Signal	Paper
Putnam & McSweeney, 2008	6	Yes	No	7	Healthy	7	5	35	Signal	PDA
Trull et al., 2008[1]	26	Yes	Yes	34	BPD	28	6	168	Signal	PDA
Wang et al., 2004	19	Yes	Unknown	267	Mixed	7	5	35	Signal	Paper
Wichers et al., 2007b	89[k]	Mixed	Unknown	422[l]	Healthy	5	10	50	Signal	Paper
Wichers et al., 2007c	89[k]	Mixed	Unknown	422[l]	Healthy	5	10	50	Signal	Paper
Wichers et al., 2009a	89[k]	Mixed	Unknown	422[l]	Healthy	5	10	50	Signal	Paper
Wichers et al., 2009b	63[a]	Yes	No	22[b]	–	12	10	120	Signal	Paper
Wichers et al., 2011	22	Yes	Unknown	–	–	42	10	420	Signal	Paper
Wichers, Lothmann, Simons, Nicolson, & Peeters, 2012	46[g]	Yes	No	39[j]	Healthy	6	10	60	Signal	Paper
Wichers, Lothmann, Simons, Nicolson, and Peeters, 2012	73[k]	No	Unknown	401[l]	Healthy	5	10	50	Signal	Paper
Children and adolescents										
Adam et al., 2010 [2]	18	Yes	Mixed	212	Mixed	3	6	18	Mixed	Paper
Axelson et al., 2003[3]	6	Yes	Yes	5[m]	Healthy	20	3	60	Signal	Phone
Cousins et al., 2011[3]	42	Yes	No	29	Healthy	8	3	24	Signal	Phone
				23	AD					
Forbes et al., 2009[3]	15	Yes	No	28	Healthy	20	3	60	Signal	Phone
Forbes et al., 2012[3]	43	Yes	No	23	AD	20	3	60	Signal	Phone
Mor et al., 2010 [2]	5	Yes	Unknown	226	Healthy	3	6	18	Signal + Time	Paper
				24	AD					
Primack et al., 2011[3]	46	Yes	No	60	Healthy	20	3	60	Signal	Phone
Silk et al., 2007[3]	19	Yes	No	16	Healthy	20	3	60	Signal	Phone
Silk et al., 2011[3]	47	Yes	No	32	Healthy	20	3	60	Signal	Phone
Whalen et al., 2008[3]	30	Yes	Yes	23	Healthy	20	3	60	Signal	Phone
Diagnosis BD										
Adults										
Depp et al., 2010	10	Yes	Unknown	0	Healthy	14	4	56	Signal	PDA
Fulford et al., 2010	12	No	Unknown	12	Healthy	21	3	63	Time	Paper
Havermans et al., 2007	38[n]	No	Yes	38[o]	Healthy	6	10	60	Signal	Paper
Havermans et al., 2010	38[n]	No	Yes	38[o]	Healthy	6	10	60	Signal	Paper
Havermans et al., 2011	36[n]	No	Yes	38[o]	Healthy	6	10	60	Signal	Paper
Husky et al., 2010	21	Unknown	Unknown	–	–	3	5	15	Signal	PDA
Knowles et al., 2007	18	No	Unknown	19[f]	Healthy	7	2	14	Time	Paper
Myin-Germeys et al., 2003	38	No	Yes	49[h]	Healthy	6	10	60	Signal	Paper
				42[i]	PD					
Children and adolescents										
Axelson et al., 2003[3]	5	Mixed	Yes	5[m]	Healthy	20	3	60	Signal	Phone call

Note: AD = anxiety disorder; BD = bipolar disorder; BPD = borderline personality disorder; MDD = major depressive disorder; mDD = minor depressive disorder; PD = psychotic disorder. PDA = personal digital assistant. Phone = phone call. Groups with identical superscript letters consist at least partially of the same individuals.

[1] Some patients did not meet the criteria for a major depressive episode but had dysthymic disorder.

[2] Youth Emotion Project.

[3] Psychobiology of Childhood Anxiety and Depression Project.

symptomatic MDD patients mood reactivity to everyday stressors may thus primarily exist at the level of NA. In this they may be different from patients with schizophrenia, who were found to be different from controls not only in how much stress increased their levels of NA but also in how much stress decreased their levels of PA (Myin-Germeys et al., 2003). Further, the finding that the association between current stress and NA is stronger in MDD has been replicated by comparing women whose twin sisters had been diagnosed with MDD to women without an MDD twin (Wichers et al., 2007). The advantage of studying the predictive value of affective stress reactions in one twin on MDD risk in the other twin is that these predictions are not confounded by the first twin's mood during the study. Wichers et al. (2007, 2009) further showed that the association between current stress and NA in women at risk for MDD was larger when they had experienced adversity during childhood yet smaller when their current levels of PA were relatively high. These findings suggest that, in MDD, high stress sensitivity in everyday life may be the result of an inherited vulnerability combined with acquired developmental challenges (e.g., childhood adversity), that may however be offset by positive events eliciting PA.

Due to their cognitive biases (Beck, 1963), MDD patients may report fewer positive events than controls and perceive these events as less pleasant and more stressful. Surprisingly, though, two groups have found that when symptomatic patients do report having recently experienced a positive event, they report *more* PA than controls, even after controlling for the perceived pleasantness and stressfulness of the event (Peeters, Nicolson, Berkhof, Delespaul, et al., 2003). Additionally, patients may report relatively *less* NA in this situation than controls (Bylsma & Rottenberg, 2011; Peeters, Nicolson, Berkhof, Delespaul, et al., 2003). A lack of positive events may thus better explain findings of low PA (and high NA) in symptomatic MDD patients than their affective reactions to these events. Indeed a lack of positive events might be especially detrimental to these patients because when these events do occur patients benefit more from them than controls.

The two research groups mentioned in this section so far have also investigated if PA and NA are associated with MDD patients' sleep quality (Bower et al., 2010; Peeters et al., 2006). While Bower et al. (2010) reported that poor sleep quality was predictive of low current levels of PA even when group status (MDD or control) was accounted for, Peeters et al. (2006) found no such association. The different results across the two studies may be explained by methodological differences between the studies in terms of the nature of the sleep quality assessment, the medication status of the study participants, and patient compliance with the ESM/EMA protocol. With respect to the existence, in symptomatic adult MDD patients, of an association between sleep quality on the one hand and PA and NA on the other hand, at this point the evidence remains inconclusive.

In the remainder of this section we will focus on how, in symptomatic MDD patients, PA and NA may be associated with their physical activity. Mata et al. (2012) observed few differences between patients and controls in the overall frequency, intensity, or duration of physical activity reported during the ESM/EMA period. When the data were analyzed in more detail, while there appeared to be no effects of physical activity on NA in either group, engaging in physical activity was found to increase PA in both patients and controls. More importantly, at the same dose level physical activity seemed to have a *larger* effect on subsequent PA in the patients. While physical activity was assessed subjectively rather than objectively, the data suggest that physical activity (like exposure to positive events, see the study by Peeters, Nicolson, Berkhof, Delespaul, et al., 2003 discussed earlier in this section) can have a direct and positive effect on symptomatic MDD patients' mood.

To summarize the data available on Topic 1, low current levels of PA and/or high current levels of NA in symptomatic adults with MDD have thus far been associated with ongoing stress and the experience of positive and negative events. These associations might help explain the observed links between low PA and high NA on the one hand and a perceived poor quality of life on the other hand. Some of the findings have been surprising, especially that symptomatic MDD patients may benefit more, not less, from positive events and physical activity than healthy controls. On the other hand, more research is necessary on how sleep may influence and be influenced by fluctuating levels of PA and NA. Nevertheless it is clear that ESM/EMA studies focusing on the contextual factors associated with affective states in MDD may be of interest to clinicians and researchers interested in the dynamics of abnormal mood and/or improving MDD treatment.

3.3. Topic 2: effects of treatment

Applying ESM/EMA to questions about the efficacy of existing biological or psychological interventions for mood disorders may also be useful, because little is known about which patients will respond. Moreover, little is known about the mechanisms of change underlying the clinical improvements that are usually, irrespective of the intervention type, reported only after several weeks. These questions have been addressed to some degree in MDD.

The first ESM/EMA study on the effects of antidepressant drugs in mood disorder patients was conducted by Barge-Schaapveld et al. (1995). The study included 21 MDD patients. Over the course of six weeks of fluvoxamine or amitryptiline treatment, their levels of PA increased and their levels of NA decreased. These changes were significant only in patients with low post-treatment clinician-rated depression scores, and may thus have been responsible for treatment responders' clinical improvement.

Barge-Schaapveld and colleagues later explored this idea further in a larger group of 63 MDD patients (Barge-Schaapveld & Nicolson, 2002; Barge-Schaapveld et al., 1999; Geschwind, Nicolson, et al., 2011; Wichers et al., 2009). As mentioned under Topic 1, during the baseline ESM/EMA period patients reported relatively little PA, a lot of NA, many physical complaints, limited enjoyment of everyday activities, and a poor quality of life (Barge-Schaapveld et al., 1999). They also reported larger NA increases after unpleasant activities than controls, while PA increases after pleasant activities were similar across the two groups (Wichers et al., 2009). Patients then received imipramine or placebo for 6 weeks. During the first week of treatment, side effects assessed using ESM/EMA were more common in the patients treated with imipramine than in patients treated with placebo. The emergence of side effects in week 1 was a positive predictor of treatment drop-out at the end of week 6, apparently because they had an immediate negative effect on patients' quality of life perceptions (Barge-Schaapveld & Nicolson, 2002). On the other hand, a significant increase in PA in week 1, representing an early response, was associated with a greater reduction in depression scores at the end of week 6 (Geschwind, Nicolson, et al., 2011). The odds of being in remission at this time were especially high if the early responders had been treated with imipramine.

In the group as a whole, depression scores after 6 weeks were lower in the patients who completed imipramine treatment than in the patients who completed placebo treatment. While quality of life assessed at the end of week 6 had on average increased to a similar degree in both groups, within-person (i.e. measurement-to-measurement or situation-to-situation) variability in quality of life measured using ESM/EMA had decreased more in the imipramine group (Barge-Schaapveld & Nicolson, 2002). Moreover, in the imipramine group PA responses to pleasant activities had increased more strongly and NA responses to unpleasant activities had decreased more strongly (Wichers et al., 2009). The magnitude of the increase in PA responses to pleasant activities from baseline was a positive predictor of being a treatment responder after 6 weeks of treatment (Wichers et al., 2009). Overall, this ESM/EMA study provides useful insights into why patients may or may not complete a treatment protocol, which aspects of everyday life are more

or less likely to change in response to pharmacotherapy, and which changes predict clinical outcome after pharmacotherapy.

More recently, Peeters et al. (2010) published ESM/EMA data on the effects of a combination of pharmacotherapy and psychotherapy (also see Wichers, Lothmann, et al., 2012). Baseline data from this group were reviewed under Topic 1 (Peeters, Nicolson, Berkhof, Delespaul, et al., 2003; Peeters et al., 2006). Patients' mood reactivity to everyday events at baseline was tested as a predictor of clinical outcome. Larger PA increases and smaller NA decreases after positive events at baseline predicted lower clinician-rated depression scores after 1 month of treatment, as did larger NA increases and smaller PA decreases after negative events at baseline (Peeters et al., 2010). Similarly, treatment response was predicted by having larger baseline NA decreases after PA increases (another measure of affective reactivity, Wichers, Lothmann, et al., 2012). Apparently patients who (still) displayed affective reactions to everyday events before treatment were more likely to improve. Notably, baseline NA responsiveness to negative events predicted remission from MDD even after 18 months (Peeters et al., 2010).

Most recently, Geschwind, Peeters, et al. (2011) reported on the effects of mindfulness training. Study participants had residual depressive symptoms after partial recovery from a major depressive episode. Patients were randomized to mindfulness training or to a waiting list. ESM/EMA was conducted before and after the intervention and involved recording PA, NA, and the pleasantness of current activities. Only patients who received mindfulness training rated their current activities as increasingly pleasant, their PA levels increased and their NA levels decreased. Most notably, they showed an increase in their PA responses to pleasant activities, an effect that was independent of reductions in NA, depressive symptoms, rumination, and worry. The extent to which PA responses to pleasant activities increased over time was a positive predictor of treatment response (Geschwind, Peeters, et al., 2011). This was especially interesting given similar findings with pharmacotherapy (Wichers et al., 2009).

As a final note we would like to refer to a letter by Wichers et al. (2011). The studies described so far used ESM/EMA to track changes in MDD patients' everyday lives in response to pharmacotherapy, psychotherapy, or a combination. Wichers et al. (2011) point out that ESM/EMA may also be used as an integral part of treatment, in that weekly summaries of patients' data can be discussed with them so they gain insight into the contexts in which they feel better or worse, and can adjust their behavior accordingly. This idea is in line with previous anecdotal reports of the positive effects of ESM/EMA on mood disorder patients' affective states and activities (Ben-Zeev et al., 2009; Donner, 1992; Husky et al., 2010). Using preliminary data from 21 mildly to moderately depressed individuals, Wichers et al. (2011) showed that their approach is both feasible and potentially helpful for MDD patients.

In summary, ESM/EMA studies have shown that PA and NA are both sensitive to treatment, that the magnitude and speed with which their levels change may predict clinical improvement, that having affective responses to emotional events at baseline might be a good prognostic tool for predicting treatment response, and that PA, NA, and affective responses to emotional events all normalize in treatment responders but not in non-responders. In this sense, ESM/EMA data can distinguish between the effects of treatment and placebo. The potential use of ESM/EMA as an integral part of treatment will be discussed in more detail in the Discussion.

3.4. Topic 3: residual symptoms in remitted patients

In the study by Barge-Schaapveld and colleagues described under Topic 2, after 6 weeks of treatment a subgroup of patients accepted continuation treatment for another 12 weeks (Barge-Schaapveld & Nicolson, 2002). By the end of week 18, there were no difference between imipramine-treated patients and placebo-treated patients in terms of clinician-rated depression scores. Nonetheless, the ESM data (but, again, not the retrospectively obtained data) showed that patients considered remitted at this point still reported more physical complaints than healthy controls and a poorer quality of life. This insight is important because lingering complaints about everyday life might be responsible for patients relapsing over time.

So far three other ESM/EMA studies have directly compared MDD patients in remission with healthy controls (Husky et al., 2009; Knowles et al., 2007; Wichers, Peeters, et al., 2012). In agreement with Barge-Schaapveld and Nicolson (2002), from these studies it appears that at least some patients continue to experience relatively high current levels of NA and stress even when they no longer meet diagnostic criteria for a current major depressive episode. When Husky et al. (2009) analyzed their data in more detail, they found that male patients in remission from MDD experienced more depressed mood following stressful events than male controls, whereas there was no such difference between female remitted patients and female controls. Stress may thus contribute to relapse in men with a history of MDD, whereas in women stress may contribute both to the development of MDD and to relapse.

The study by Wichers, Peeters, et al. (2012), like that of Mata et al. (2012) discussed under Topic 1, explored links between MDD patients' affective states and physical activity, but in this case the patients were in remission. Like in the study by Mata et al. (2012), there were no differences between patients and controls in the overall level of self-reported physical activity, there were no effects of physical activity on NA in either group, and physical activity increased PA in both groups. However, unlike in the study by Mata et al. (2012), physical activity seemed to have a *smaller* effect on subsequent PA in the patients than in the controls. This suggests that patients in remission may be less motivated to continue exercising after recovery from a depressive episode, even though they are relatively sensitive to the positive effects of physical activity during the episode (Mata et al., 2012). Exercise may be more effective in the acute treatment phase of MDD than in the relapse prevention phase.

In summary, ESM/EMA studies in remitted MDD patients have identified various residual symptoms that may over time contribute to relapse: lingering complaints about physical symptoms and a poor quality of life (Barge-Schaapveld & Nicolson, 2002) chronic high levels of NA and stress (Husky et al., 2009; Knowles et al., 2007), and perhaps a low motivation to engage in physical activity (Wichers, Peeters, et al., 2012).

3.5. Topic 4: findings specific to pediatric populations

So far we have limited our review to adults with MDD. However, two large and currently still ongoing research projects have generated ESM/EMA data specifically in pediatric populations with mood disorders, mostly MDD: the Psychobiology of Childhood Anxiety and Depression Project and the Youth Emotion Project. Given age-related differences in the clinical presentation of mood disorders (e.g., Kovacs, 1996; Leibenluft et al., 2003), ESM/EMA studies in children and adolescents with MDD and BD may provide insight in how their everyday lives, which tend to differ substantially from those of adults, may influence their symptoms, or be influenced by them. Here we review ESM/EMA data obtained from MDD youth. Data obtained from BD youth are reviewed under Topic 5.

In the Youth Emotion Project, Mor et al. (2010) used ESM/EMA to measure affect and self-focused thinking in a large group of adolescents, 10 of whom had a current unipolar depression (5 had MDD). In this group, unlike in depressed adults (see Topic 1), being depressed was generally not associated with higher levels of NA. However, when depressed youth engaged in self-focused thinking, they were more likely to report NA than non-depressed youth (Mor et al., 2010). This suggests that high levels of NA in pediatric MDD

may only occur in certain contexts. This context specificity might disappear when patients become adults. These results highlight the importance of considering context when evaluating patients' affective states, something that is more difficult in studies using retrospective mood assessments.

In the Psychobiology of Childhood Anxiety and Depression Project, rather than engaging participants in signal-contingent data recording, ESM/EMA data are being collected using repeated, pseudo-randomly scheduled, phone interviews administered by the investigators. This is done to improve the quality of the data. Axelson et al. (2003) published the first ESM/EMA data from this project. Compared to healthy controls, MDD youth were more than twice as likely to report being alone at the time of a phone interview. Moreover, they reported fewer planned activities, less PA, and more NA. More recent publications from the project have included reports on affective states and sleep (Cousins et al., 2011), on sleep, daily caffeine consumption, and nervousness (Whalen et al., 2008), and on media use (Primack et al., 2011). Moreover, Silk et al. (2011) and Forbes et al. (2012) recently published ESM/EMA data on the effects of treatment in MDD youth.

ESM/EMA data on affective states and sleep in adults with MDD were previously described by Peeters et al. (2006) and Bower et al. (2010) and are summarized under Topic 1. Bower et al. (2010) reported worse sleep quality in the MDD group than in a control group, which predicted low daily levels of PA. According to Cousins et al. (2011), youth with MDD can also be characterized by sleep problems. However, in this group low daily levels of PA were found to be associated with a *longer* subsequent sleep. Moreover, a longer sleep was associated with *higher* levels of PA the following day. Further, higher daily levels of NA were associated with *less* subsequent night-time wakefulness, and less night-time wakefulness was associated with *lower* NA levels the following day. These associations were not seen in the control group (or in youth with anxiety disorders). These data are interesting because they suggest a restorative effect of sleep after days during which MDD youth experienced a worse mood. No such effect was apparent in the adult patients (Bower et al., 2010; Peeters et al., 2006). This suggests that promoting sleep hygiene (Berk, 2009) might benefit youth with MDD more than adults with MDD. However, since the adult and youth findings were based on different sleep measures and data analyses, inferences drawn from them remain speculative.

Whalen et al. (2008) have also reported subjective sleep quality to be relatively poor in MDD youth. One factor that may contribute to poor sleep quality is caffeine consumption, which most people start in adolescence. However, while MDD youth were found to consume more caffeine than aged-matched controls, there appeared to be no significant association either between daily caffeine consumption and subsequent sleep or between sleep and subsequent caffeine consumption. Nonetheless, since caffeine consumption in the MDD group was positively associated with nervousness, this group may have differed from the control group in caffeine consumption, and possibly in sleep quality, due to comorbid anxiety disorders in some patients.

Another recent publication from the Psychobiology of Childhood Anxiety and Depression Project is an especially good example of how ESM/EMA can be adapted to suit the population under study. Children and adolescents use different types of media than adults, and Primack et al. (2011) found that MDD youth favored listening to music over reading more than non-depressed youth. It is unfortunate that the data were not analyzed in more detail and/or linked to participants' levels of PA and NA. Also, future studies could explore to what extent MDD youth might choose various types of media to complement or counteract their mood.

Finally, ESM/EMA data on the effects of treatment in MDD youth participating in the Psychobiology of Childhood Anxiety and Depression Project have recently been published by Silk et al. (2011) and Forbes et al. (2012). Treatment consisted of pharmacotherapy, psychotherapy, or both. Silk et al. (2011) reported that, at baseline, patients had higher mean levels of NA than controls, including more sadness, anger, and nervousness, and also more variability in their NA levels. Moreover they spent a relatively small proportion of their time in the presence of other people. Over the course of treatment, MDD youth showed a decrease in both mean levels of and variability in NA. Specifically, they became less sad and angry. Interestingly, they did not become less nervous and the amount of time they spent alone also did not change. Further, Forbes et al. (2012) reported that patients with lower levels of NA and higher mean levels of PA at baseline were more likely to improve with treatment. Moreover, patients who spent more time with their fathers were more likely to recover, whereas patients who spent more time with peers were less likely to recover. Since the social lives of children and adolescents with MDD are likely to differ from those of adults with MDD, these data again provide a good example of how ESM/EMA may be useful in elucidating the factors that contribute to mood disorders and the success of treatment in youth.

In summary, there are several good examples of how ESM/EMA may be employed to increase insight in the everyday lives of children and adolescents with MDD. Most notably, studies have focused on caffeine consumption, media use, and time spent with others. In this age group, relationships with peers and (potential) romantic partners are often unstable (Zimmer-Gembeck, 1999). Therefore, future ESM/EMA studies in MDD youth could focus more on social functioning. We return to this topic in the Discussion.

3.6. Topic 5: findings specific to bipolar disorder

The number of ESM/EMA studies in BD patients is still limited (see Table 1). Nonetheless, a comparison with data from MDD patients may provide insights in how the groups differ in everyday life.

The study by Knowles et al. (2007) mentioned previously under Topic 3 included not only remitted MDD patients and controls, but also remitted BD patients. As might have been expected based on their clinical status, levels of PA, NA, and self-esteem did not reliably differentiate the BD group from the control group. However, patients had relatively high levels of within-person variability in all three variables, even though they did not report more or more intense everyday events. Additionally, variability in PA and self-esteem distinguished BD from MDD, but variability in NA did not.

The comparison between BD patients, MDD patients, and healthy controls conducted by Myin-Germeys et al. (2003) is based on the largest number of participants to date. Moreover, few ESM/EMA studies obtained more repeated measures per participant. Patients with BD (mostly type 1) reported larger decreases in PA when stressed than controls. There was no such group difference for NA, which is especially interesting given that patients with MDD reported larger increases in NA when stressed than controls, without there being such a group difference for PA. While these findings suggest a double dissociation with respect to affective reactions to stress in BD and MDD, it should be noted that BD patients were in remission while MDD patients were symptomatic.

Additional data on the BD patients have been published by Havermans and colleagues, using a different control group (Havermans et al., 2007; Havermans et al., 2010). During the ESM/EMA period participants recorded not only their levels of PA and NA, but also what they were doing and if they had experienced any positive and negative events since the previous signal. On average BD patients reported less PA and more NA than the controls (Havermans et al., 2010), and spent more time at home, alone, and/or engaged in passive activities such as watching television (Havermans et al., 2007). At the same time, BD patients reported positive and negative events as often as controls and found them equally stressful (Havermans et al., 2007). Nonetheless, more detailed analyses revealed that a subgroup of patients with mild depressive symptoms experienced negative events as more stressful

than controls (Havermans et al., 2007). This may help explain why this subgroup showed relatively large increases in NA following negative events (Havermans et al., 2010). Stressful events might be a risk factor for depressive relapse in BD.

So far the Psychobiology of Childhood Anxiety and Depression Project has been the only one to include an ESM/EMA study in youth with BD (Axelson et al., 2003). As a group, BD youth reported less PA and more NA than controls. Also they were relatively unlikely to report planned activities. In these ways they were similar to MDD youth (described under Topic 4). The difference from MDD youth was that BD youth were less likely to report being alone. Unfortunately the number of patients studied by Axelson et al. (2003) was small. However, in addition to group-level data, Axelson et al. (2003) presented several patients individually. These data provide support for the idea that ESM/EMA might benefit not only groups of mood disorder patients but also individuals on a case-by-case basis (cf. Wichers et al., 2011).

Two recent papers further highlight the feasibility of ESM/EMA in BD and the possibilities it creates for studying and possibly even treating this disorder. Using a signal-contingent data recording approach, Fulford et al. (2010) obtained ESM/EMA data from adult BD patients in remission and controls on how close they felt towards reaching three self-identified goals at the time of each data recording, on how much effort they had put towards these goals since the previous recording, and on how much closer they expected to get to obtaining these goals by the next recording. As expected, both groups of participants reported an increase in future effort after making less progress towards a goal than expected based on past effort, and vice versa. However, in the BD group unexpected progress towards a goal reduced future effort less than in the control group. This finding was interpreted as a potential indicator of patients' risk of relapse into mania.

Lastly, Depp et al. (2010) tested a PDA for repeatedly assessing mood in BD patients with the goal of providing real-time personalized suggestions for health-promoting behaviors when patients report an increase in their symptoms. The overall occurrence of depressive and manic symptoms during the ESM/EMA period correlated with patients' scores on traditional mood rating scales. Using the PDA for up to 2 weeks resulted in a decrease in clinician-rated depression scores and patients felt strongly that continuing to use the PDA would be helpful to them. The approach taken by Depp et al. (2010) in BD patients resembles that of Wichers et al. (2011) in MDD patients. Depp et al. (2010) and Axelson et al. (2003) are so far the only two studies to include BD patients not in remission.

In summary, a small number of ESM/EMA studies have been conducted in BD patients. Some studies have directly compared BD to MDD. Several differences between the two groups with respect to variability in PA and NA have been reported, but these may be explained by clinical status differences. To gain insight into why (hypo)manic episodes are recurrent in most BD patients, one study used ESM/EMA to look at how patients pursue their everyday goals. Another study suggests that clinicians working with BD patients might be interested in using ESM/EMA in the context of psychoeducation.

3.7. Topic 6: the neuroscience of mood disorder patients' everyday lives

The inclusion of biological variables in ESM/EMA goes back to the 1980s, when researchers started using ambulatory devices for the continuous monitoring of cardiovascular activity (Shiffman et al., 2008). Studies including measures of brain function are a more recent phenomenon. Most notably, and in line with current theories about the underlying neurobiology of MDD (aan het Rot, Mathew, & Charney, 2009), there has been an interest in the hypothalamic–pituitary–adrenal (HPA) system and in prefrontal and striatal brain activity.

Peeters and colleagues are so far the only group to have studied, in adults with MDD, HPA system functioning in the context of ESM/EMA (Peeters, Nicolson, & Berkhof, 2003). This was done by repeatedly obtaining saliva from study participants and subsequently measuring salivary levels of cortisol, considered a marker of HPA system functioning (Peeters, Nicolson, Berkhof, Delespaul, et al., 2003). Compliance rates suggested that repeatedly obtaining saliva in the context of ESM/EMA had not been problematic. Mean cortisol levels in the MDD patients were not significantly different from mean cortisol levels in the controls, but within-person variability in cortisol was higher in the MDD group (Peeters, Nicolson, & Berkhof, 2004). Moreover, in this group, unlike in the control group, cortisol levels did not significantly increase following everyday negative events (Peeters, Nicolson, & Berkhof, 2003). This is especially interesting given that MDD patients experience these events as relatively unpleasant and stressful (Peeters, Nicolson, Berkhof, Delespaul, et al., 2003). Together these results point towards a dysfunction of the HPA system in responding to daily hassles.

Additional cortisol data are available in MDD youth (Adam et al., 2010) and in adults with BD (Havermans et al., 2011). Participants enrolled in the Youth Emotion Project (see Topic 4) completed an ESM/EMA protocol that included repeated assessments of NA and fatigue as well as salivary cortisol. Adolescents who in the following year experienced a major depressive episode had an elevated cortisol awakening response and relatively high mean levels of current fatigue (but not NA) at baseline (Adam et al., 2010). Unfortunately, the authors did not report whether fatigue levels and cortisol awakening responses were correlated. Moreover, pre-existing psychological and physiological abnormalities might at least partially explain the findings, since some of the adolescents who became depressed already had a lifetime MDD diagnosis at baseline.

The remitted BD patients studied by Havermans et al. (2011), like the symptomatic MDD patients studied by Peeters et al. (2004), did not have abnormal mean daily cortisol levels. However, unlike the MDD patients, the BD patients displayed a rather flat decline in salivary cortisol levels throughout the day. Cortisol reactivity to negative everyday events was blunted in a subgroup of BD patients with many past mood episodes, like it was in the MDD patients (Peeters, Nicolson, & Berkhof, 2003), whereas BD patients with few past episodes displayed normal cortisol reactivity to negative everyday events. This suggests that, in BD, recurrent mood episodes may over time exacerbate abnormal HPA responses to daily hassles.

The remaining ESM/EMA studies to include neurobiological variables have used a single baseline measure rather than measure these variables repeatedly over time. One such study was conducted in adults with MDD (Putnam & McSweeney, 2008). At the beginning of the study prefrontal brain function was measured using electroencephalography (EEG). Subsequent rumination measured during a one-week ESM/EMA period was higher and self-esteem was lower in patients with less prefrontal neural activity. In healthy controls there were no significant associations between the strength of the EEG signal and rumination and self-esteem. Thus, prefrontal brain dysfunction may be associated with everyday cognitive symptoms in MDD.

Brain function was also assessed in MDD youth participating in the Psychobiology of Childhood Anxiety and Depression Project (see Topic 4). Forbes et al. (2009) used functional magnetic resonance imaging (fMRI) to measure neural activity while study participants completed a computer task involving their anticipation of and exposure to monetary rewards. In this study the fMRI session took place *after* participants completed a four-day ESM/EMA period during which data were collected on their current levels of PA and NA. Forbes et al. (2009) did not explicitly report differences in mean PA levels between youth with and without MDD, but other publications on the cohort (Axelson et al., 2003; Cousins et al., 2011) suggest that the MDD group reported less PA than the healthy control group. Lower mean levels of PA were associated with less activation in striatal areas during reward anticipation and exposure, specifically in the left caudate. It was therefore not surprising that left caudate

activation during reward processing was lower in the MDD group than in the control group. No associations between striatal activity and NA were reported.

Nonetheless, a link between a physiological measure obtained in the lab and NA assessed in everyday life has been reported by another study from the Psychobiology of Childhood Anxiety and Depression Project (Silk et al., 2007). Participants underwent pupillometry while completing a word valence identification task. The pupil is known to become more dilated in response to more emotionally intense stimuli (Siegle, Steinhauer, Carter, Ramel, & Thase, 2003). Pupil dilation 5–10 s after identifying a presented word as negative was less pronounced in youth with MDD compared to healthy controls. Task performance was considered a valid lab measure of everyday life function because study participants with less pronounced pupil dilation responses reported more NA and less PA during ESM/EMA. As pupil dilation responses to negative stimuli are considered a measure of the emotional reactivity of the brain, this suggests that MDD youth with higher levels of NA and lower levels of PA are less emotionally reactive. Given the focus on reactivity, future studies might additionally explore possible associations between task performance and the magnitude of NA and PA responses to recent everyday events.

In summary, ESM/EMA studies in mood disorder patients exploring links between everyday functioning and the brain have so far mostly focused on cortisol. Other brain variables have been explored, but due to their nature most have been assessed in a laboratory setting shortly before or after the ESM/EMA period and tested as predictors of everyday functioning.

4. Discussion

4.1. General summary

Most ESM/EMA studies in mood disorder patients have focused on adults with MDD (Table 1). Major findings in this population include associations between low PA and high NA and the experience of positive and negative everyday events (Topic 1), the normalization of affective responses to emotional events during treatment (Topic 2), and the continued presence of subtle abnormalities such as high NA even after treatment that is considered successful from a clinical perspective (Topic 3). In MDD youth ESM/EMA has provided several insights into the factors influencing the flow of their everyday lives, such as time spent with others (Topic 4). ESM/EMA studies in BD patients have highlighted how they are in some ways similar to but in other ways different from MDD patients with respect to the factors that may influence their everyday levels of PA and NA (Topic 5). Moreover, changes in PA and NA in response to emotional events may influence cortisol levels differently in MDD patients than in BD patients; cortisol is currently the only neurobiological variable to have been added directly to ESM/EMA protocols (Topic 6).

4.2. Rationale for using ESM/EMA for the study of mood disorders

In the past 20 years, there has been a steady increase in the number of papers on ESM/EMA in patients with mood disorders. A primary reason for choosing ESM/EMA over other available methods for the study and monitoring of MDD symptoms has been that depressed patients may be negatively biased in their recall of past states and events and overestimate their level of symptoms and stress (Beck, 1963). ESM/EMA limits the impact of this recall bias by studying patients in real-time. Several studies have directly compared ESM/EMA with a retrospective assessment. Mokros (1993) found that depressed adolescents were not necessarily more likely than controls to report sadness and irritability in real-time, yet they were more likely to report these symptoms retrospectively. However, Ben-Zeev et al. (2009) found that while MDD patients retrospectively overestimated how high their levels of NA had been in real-time, controls did so to a similar degree. Moreover, in the study by Bylsma et al. (2011), MDD patients and controls both reported *less* NA retrospectively than in real-time. It seems that a negative recall bias in MDD might exist mostly in terms of the underreporting of PA. Mokros (1993) found that, compared to healthy controls, depressed adolescents were also more likely to report anhedonia retrospectively than in real-time and Ben-Zeev et al. (2009) found that MDD patients were less likely than healthy controls to retrospectively overestimate their levels of PA. Yet Bylsma et al. (2011) found that MDD patients and healthy controls reported less PA retrospectively to a similar degree, and so at this point the data remain inconclusive.

Nonetheless there are several additional reasons for choosing ESM/EMA for the study of mood disorders. Most importantly, the intensive, repeated assessment of mood disorder patients enhances insight into the everyday correlates of their symptoms. For example, ESM/EMA data from Peeters, Nicolson, Berkhof, Delespaul, et al. (2003) suggest that low PA and high NA in adults with MDD are more closely associated with the absence of positive daily events than with the presence of negative events. Further, current stress in MDD may be more closely linked to high NA than to low PA (Myin-Germeys et al., 2003). Data from studies that have looked at PA and NA in relation to sleep suggest that sleep might be mood-restorative in youth with MDD (Cousins et al., 2011), but not or no longer in adults with MDD (Bower et al., 2010; Peeters et al., 2006). Finally, stress in BD patients appears more closely linked to low PA than to high NA (Myin-Germeys et al., 2003) but a subgroup with mild depressive symptoms shows large increases in NA following exposure to negative events (Havermans et al., 2010), which they experience as relatively stressful (Havermans et al., 2007). Thus, ESM/EMA studies in mood disorder patients can help elucidate what aspects of everyday life contribute to their disordered mood, and these studies can be tailored to the population studied.

Additionally, ESM/EMA can provide insight into the influences treatment has on patients' everyday lives and vice versa. Geschwind, Nicolson, et al. (2011) found that MDD patients who reported an increase in PA during the first week of treatment were less depressed after 6 weeks of treatment. On the other hand, Barge-Schaapveld et al. (1999) found that experiencing side effects in the first week of treatment made MDD patients less likely to complete the treatment. This highlights the value of using ESM/EMA during treatment to help increase our understanding of the everyday life changes that may promote or prevent clinical improvement. ESM/EMA studies may also improve the measurement of mood disorder treatment effectiveness: both Wichers et al. (2009) and Geschwind, Peeters, et al. (2011) have found that being a responder after 6 weeks of treatment for MDD was associated with a large increase in the magnitude of PA responses to pleasant activities, an everyday life measure of the absence of anhedonia. Further, ESM/EMA might help identify predictors of treatment success in mood disorder patients: according to Peeters and colleagues (Peeters et al., 2010; Wichers, Lothmann, et al., 2012), MDD patients whose everyday affective responses are more “normal” before treatment are more likely to improve. The findings described above were conducted at group level; it would be interesting to explore if similar trends are seen at the level of individual patients. As highlighted in several small studies, ESM/EMA data that are fed back to individual patients close in time to their recording may give them insight into the factors that influence their everyday moods and could therefore be therapeutic (Axelson et al., 2003; Depp et al., 2010; Wichers et al., 2011). ESM/EMA could be incorporated in existing treatment options.

Further, ESM/EMA studies might be used to assess residual symptoms in remitted mood disorder patients. The data from Barge-Schaapveld and Nicolson (2002) and Husky et al. (2009) suggest that while MDD patients in remission may appear similar to controls at a global level of functioning, ESM/EMA can still reveal subtle abnormalities that could potentially contribute to future relapse. BD patients in remission are also different from healthy controls (Knowles

et al., 2007; Myin-Germeys et al., 2003). Increased awareness of continuing abnormalities in seemingly remitted mood disorder patients may help prevent another major depressive or manic episode.

Finally, ESM/EMA can be used to study the neuroscience of everyday functioning in mood disorder patients. Some studies have associated aspects of everyday life measured using ESM/EMA with brain function measured on a single occasion in a lab setting (Forbes et al., 2009; Putnam & McSweeney, 2008; Silk et al., 2007). This is not ideal, but the intensive repeated measurement of brain function using pupil dilation, EEG, or fMRI is not feasible. Nonetheless, in some cases the intensive repeated measurement of psychological and physiological variables together is feasible, such as when obtaining salivary cortisol for the assessment of HPA system functioning (Adam et al., 2010; Havermans et al., 2011; Peeters, Nicolson, Berkhof, Delespaul, et al., 2003). Additional options are discussed later in this section.

4.3. Limitations at the level of ESM/EMA data collection, analysis, and interpretation

A first limitation of most ESM/EMA studies in MDD and BD patients to date is that patients' reporting of their everyday lives may be confounded by their mood disorder. For example, in the studies by deVries and colleagues (e.g., Havermans et al., 2010; Peeters, Nicolson, Berkhof, Delespaul, et al., 2003), the same type of event might have been stressful and thus reported by patients but not by healthy controls. Conversely, as discussed by Wenze and Miller (2010), patients in signal-contingent data recording studies may underreport symptoms if they miss signals during periods when they are more symptomatic. Indeed, while participant acceptance of ESM/EMA studies may be high in mood disorder patients seeking treatment through outpatient clinics (Husky et al., 2010), patients who are severely ill may be relatively unlikely to participate. Or, they may be medicated which might also confound their data. Nonetheless, in these respects ESM/EMA is not much different from more traditional methods to assess mood disorder patients.

So far all ESM/EMA studies in mood disorder patients have employed a signal- or time-contingent data recording approach. While this may eliminate recall bias when patients are asked about their current affective state, in several studies they have also been asked about recent events. Signal- and time-contingent recording may result in a substantial lag between the timing of an event and patients' reporting of it. In the meantime patients' appraisal of the event may be significantly altered. For example, if between two recordings a verbal disagreement with another person occurs and is followed by reconciliation, then patients may report the quarrel as less stressful than it actually was, or even not report it at all. The likelihood of this occurring may be reduced by using an event-contingent data recording approach where social interactions are the events of interest. So far no ESM/EMA studies have used this approach in mood disorder patients, even though methods for the event-contingent recording of affect, cognitions, and behaviors occurring during social interactions do exist (Knee, Canevello, Bush, & Cook, 2008; Moskowitz, 1994; Moskowitz et al., 2009). Social interactions are events that are certainly relevant to mood disorder patients (Hirschfeld et al., 2000; Joiner & Timmons, 2008) and they are common enough to be suitable for investigation using ESM/EMA. As noted by Ebner-Priemer and Trull (2009), this is not true for all types of events, such as suicide attempts. Moreover, a limitation of event-contingent recording is that, given the absence of pager signals, it depends more than signal-contingent recording on the intrinsic motivation of patients.

To date ESM/EMA data collected in mood disorder patients and other groups have mostly been analyzed using group-level comparisons. This is unfortunate because group-level comparisons may mask strong associations between symptoms and contextual variables in individual patients. For example, different MDD patients may show different PA responses to physical activity. While between-group comparisons are very suitable for generalizing to the MDD population at large, when this type of data aggregation is employed, within-person heterogeneity is easily obscured (Molenaar & Campbell, 2009). Conventional group designs may therefore be of limited value to the development of effective personal interventions, e.g. exercise for patients who show PA increases after physical activity but not for patients who do not (Hamaker, Dolan, & Molenaar, 2005). To overcome this, a multivariate time-series design may be employed using repeated observations in single persons. ESM/EMA is well tailored to provide such data. The temporal dynamics between two or more variables may be investigated using vector auto-regression (VAR) models. This way complex relationships between variables can be unraveled, such that it becomes possible to make inferences about person-level cause–effect relationships (Wild et al., 2010). VAR modeling would be quite useful for both research and clinical practice as a means to determine the specific factors associated with mood symptoms in individual patients (Rosmalen, Wenting, Roest, de Jonge, & Bos, 2012). In other words, ESM/EMA may come to play an important role in personalized medicine.

With respect to data analytic issues, it should also be noted that ESM/EMA studies tend to recruit a substantial number of participants who commit a significant amount of time and generate a lot of data. This can make these studies labor intensive and expensive. Fortunately they have the potential to generate several new insights in the population studied thanks to the intensive repeated measurement of multiple variables. However, many researchers are unfamiliar with the optimal statistical analysis of ESM/EMA data or focus on mean levels without considering variation around the mean (Ebner-Priemer, Eid, Kleindienst, Stabenow, & Trull, 2009; Gueorguieva & Krystal, 2004; Schwartz & Stone, 1998). Moreover, few researchers seem to return to their data for secondary analyses after their primary findings have been published even though over time new questions may arise that existing ESM/EMA data sets might be able to answer. To illustrate this, consider two ESM/EMA studies that measured the impact of increasing serotonin on mean levels of interpersonal behaviors during social interactions (aan het Rot, Moskowitz, Pinard, & Young, 2006; Moskowitz, Pinard, Zuroff, Annable, & Young, 2001). These studies were later combined to explore how alcohol might influence interpersonal behavior (aan het Rot, Russell, Moskowitz, & Young, 2008b). It would not have been possible to adequately test this in one data set alone because participants generally reported few social interactions involving alcohol. After developing the construct of interpersonal spin as a measure of within-person variation in interpersonal behavior (Moskowitz & Zuroff, 2004), the studies were again combined to assess the impact of increasing serotonin on spin (Moskowitz, Zuroff, aan het Rot, & Young, 2011). To reduce the cost and enhance the impact of an ESM/EMA study, researchers should be encouraged to publish additional findings from combined data sets or novel types of analyses.

A final potential limitation of many of the ESM/EMA studies reviewed here pertains to the ongoing debate on the independence of PA and NA within a given situation (see also the Introduction). In the context of our review, we provide here some ESM/EMA data on this issue. Larson (1987) asked adolescents and adults to complete semantic differential scales of affective state for 1 week, in response to pager signals occurring randomly every 2–3 waking hours. Levels of PA and NA on consecutive data record forms were not significantly correlated in either age group. Rafaeli, Rogers, and Revelle (2007) asked groups of students to complete visual analog mood scales every three waking hours for 5–14 days. Within-person correlations of PA and NA showed considerable variability but across participants averaged around zero. They were not predicted by personality factors thought to predispose to mood disorders, such as neuroticism. Participants with stronger negative within-person correlations of PA and NA indicated that they tend to focus more on the (un)pleasantness

of affect items rather than their arousal, but it is unclear to what extent mood disordered patients might have more or less valence focus than controls. Together these studies suggest that the within-person interdependence of PA and NA that has been observed in other types of studies may not influence interpretation of the findings of the ESM/EMA studies reviewed here; however future studies might specifically look into this issue.

Additional issues with ESM/EMA in mood disorder patients include the current lack of standardized data record forms (though see Moskowitz, 2005; Moskowitz et al., 2009; Moskowitz & Young, 2006), limited experimental control of confounding variables, and the subjectivity of participants' self-reports. These have previously been discussed by Ebner-Priemer and Trull (2009) and Wenze and Miller (2010).

4.4. Opportunities for the future

There are several points on which future ESM/EMA studies may focus. In this final section of the Discussion we concentrate on points we believe are most relevant to clinicians. Additional points, such as the need to validate the various approaches used to date, the standardization of data record forms, the use and continued development of advanced analytic strategies for data, and the ethical dilemmas that may surround studies in mood disorder patients, have been discussed elsewhere (Ebner-Priemer & Trull, 2009; Ebner-Priemer et al., 2009; Moskowitz & Young, 2006; Wenze & Miller, 2010).

Many ESM/EMA studies in MDD and BD have focused on PA and NA in the context of self-appraised positive and negative everyday events. While the results from these studies have increased insight into the vicissitudes of the lives of mood disorder patients, it can be argued that asking patients to report all recent positive and negative events may not be ideal, for example because definitions about what constitutes an emotional event may vary from person to person. To be able to generalize across patients, we feel a better approach may be to ask patients to only report on certain well-defined events. One example would be to ask patients to report on their affect when smoking a cigarette (Shiffman, 2009). In the context of interpersonal theories of depression (Joiner & Timmons, 2008) and widespread evidence of social impairments in depressed patients (Hirschfeld et al., 2000), another example would be to ask patients to report on their conversations with others. In the only ESM/EMA study to take this approach to date, one not included in our systematic review because participants were not assessed more than once per day, symptomatic MDD patients completed a variant of the Rochester Interaction Record daily for about 2 weeks and were found to report a poorer social interaction quality compared to healthy controls (Nezlek, Hampton, & Shean, 2000). Unfortunately, the study used a time-contingent approach for recording social interactions whereas to avoid memory bias an event-contingent approach might have been preferable.

Such an approach has been used in an ESM/EMA study in healthy adults with low or higher scores on a depression rating scale (Zuroff, Fournier, & Moskowitz, 2007). Participants with higher depression scores reported more submissive and fewer dominant behaviors than participants with low scores. Moreover, compared to these low scorers, the high scorers changed their interpersonal behavior differently in response to interacting with others perceived as dominant and/or agreeable. The event-contingent recording of social interactions in this study was accomplished using a validated method (Moskowitz, 1994). It was designed for the real-time assessment of interpersonal behavior but has also been used to measure people's perceptions of the behavior of their interaction partners, as well as PA and NA in the context of social interactions (for a review, see Moskowitz, 2005). The method has previously been used in adults with borderline personality disorder and social phobia (Russell, Moskowitz, Zuroff, Sookman, & Paris, 2007; Russell et al., 2011). Other data obtained using this method are suggestive of abnormal gender-specific patterns of social functioning in children of BD patients (Linnen, aan het Rot, Ellenbogen, & Young, 2009). Together these data support the event-contingent recording of mood disorder patients' social interactions. Findings obtained from these ESM/EMA studies might increase insight into the nature of patients' impairments in social functioning (Hirschfeld et al., 2000; Joiner & Timmons, 2008) and how these may be reduced during treatment.

Indeed, another opportunity for ESM/EMA in the context of mood disorders research is created in the context of the delayed onset of action of most currently available antidepressants. Harmer, Goodwin, and Cowen (2009) have suggested that their clinically therapeutic effects, usually only reported 2–6 weeks into treatment, may be explained by acute but very subtle changes in emotional processing that accumulate over time. ESM/EMA data recorded in MDD patients in the first week of antidepressant treatment have shown that an increase in PA in this week may be predictive of clinical improvement after the sixth treatment week (Geschwind, Nicolson, et al., 2011). In the future, ESM/EMA could be employed throughout these six weeks of treatment, or at least throughout the first 2 weeks. It would be interesting to study changes in PA and NA over this time in more detail. Moreover, it would be interesting to see if patients become more agreeable and less quarrelsome during their social interactions (and this might be associated with the early increase in PA reported by Geschwind, Nicolson, et al., 2011). For serotonergic antidepressants this might be expected based on two previous ESM/EMA studies in which serotonin was increased in healthy people, some of whom were likely at risk for future MDD (aan het Rot et al., 2006; Moskowitz et al., 2001). Over time, during the course of treatment, interaction partners may be expected to adjust their behavior accordingly, thereby improving the overall quality of patients' social interactions with people in their environment. Patients may then start feeling more PA and less NA during their social interactions and this might further increase their agreeableness and decrease their quarrelsomeness. It is likely that such subtle psychological changes occur well before patients become consciously aware of their improved mood. This might help explain why most antidepressants have a delayed onset of action.

Future ESM/EMA studies on the effects of serotonergic antidepressants may not only increase insight into the everyday life changes that ultimately contribute to its therapeutic effects, but also further elucidate in MDD patients the role of serotonin in the regulation of mood and social interactions (cf. Moskowitz & Young, 2006). This would be one way to advance knowledge on the neuroscience of everyday life. Other options that could be explored further include using ESM/EMA in the context of positron emission tomography of the serotonin or dopamine system (Martinot et al., 2001; Rosa-Neto et al., 2004). The finding of Forbes et al. (2009) that MDD youth who reported less PA during ESM/EMA showed less neural activation in the striatum could be interpreted as a link between dopamine abnormalities and an everyday measure of anhedonia in this group. As implied by Wichers, Aguilera, et al. (2007), ESM/EMA studies in mood disorder patients that consider polymorphisms in neurotransmitter-related genes could also be interesting.

Additional brain–behavior links that could be explored in mood disorder patients using ESM/EMA include light exposure and physical activity; both are thought to be beneficial to patients with MDD (aan het Rot, Collins, & Fitterling, 2009a; Golden et al., 2005) and very sensitive, non-invasive, and ecologically valid methods for measuring light exposure and physical activity continuously and in real-time are available for this purpose (aan het Rot, Moskowitz, & Young, 2008a; Jones, Tai, Evershed, Knowles, & Bentall, 2006). Finally, while ESM/EMA is currently still limited in the range of physiological variables that can be measured repeatedly in everyday life, one potential example relevant to MDD is blood pressure (Kamarck et al., 2005). Ilies, Dimotakis, and Watson (2010) previously measured blood pressure in the context of an ESM/EMA study of PA and NA in university

employees. Participants were asked to activate a blood pressure monitor every time they made a PA and NA recording. Ilies et al. (2010) found that when NA was higher, blood pressure was higher, without any association between PA and blood pressure. These results resemble those of D'Antono, Ditto, Moskowitz, and Rios (2001) who measured blood pressure on a single occasion at baseline and found that women with a higher blood pressure subsequently reported more submissive behaviors and fewer agreeable behaviors. Moreover, an ESM/EMA study by Kamarck et al. (2002) has shown that blood pressure, measured repeatedly using an ambulatory monitor, increases during periods of psychosocial stress, measured repeatedly using the Diary of Ambulatory Behavioural States. Adding the repeated measurement of blood pressure (and heart rate, for which ambulatory devices are also available) to ESM/EMA studies of MDD patients may ultimately help explain why they are at risk for cardiovascular disease (van der Kooy et al., 2007). The fact that ESM/EMA data collection takes place in people's natural environments is a tremendous advantage because it facilitates generalization to real life.

4.5. Summary and conclusion

We have systematically reviewed all published ESM/EMA studies conducted in patients with MDD and BD (Table 1). We have focused on everyday correlates of the disordered mood these patients display, shown how ESM/EMA has been used in the context of treatment, distinguished findings in remitted patients from those in symptomatic patients, differentiated between adult and pediatric populations, and summarized the available data on the links with neuroscience. The studies conducted to date have several implications for mental health researchers and clinicians, and many opportunities for future studies remain. ESM/EMA in mood disorder patients aims to help understand the dynamics of their everyday lives. Perhaps most notably, the insights obtained from ESM/EMA may not only serve researchers and clinicians, but might also benefit patients directly.

5. Declaration of interest

The authors declare no conflicts of interest in relation to this paper.

Acknowledgment

Dr. aan het Rot is supported by the Innovational Research Incentives Scheme Veni from the Netherlands Organisation for Scientific Research (NWO).

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