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Ambulatory Assessment

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Abstract

Ambulatory assessment (AA) covers a wide range of assessment methods to study people in their natural environment, including self-report, observational, and biological/physiological/behavioral. AA methods minimize retrospective biases while gathering ecologically valid data from patients' everyday life in real time or near real time. Here, we report on the major characteristics of AA, and we provide examples of applications of AA in clinical psychology (*a*) to investigate mechanisms and dynamics of symptoms, (*b*) to predict the future recurrence or onset of symptoms, (*c*) to monitor treatment effects, (*d*) to predict treatment success, (*e*) to prevent relapse, and (*f*) as interventions. In addition, we present and discuss the most pressing and compelling future AA applications: technological developments (the smartphone), improved ecological validity of laboratory results by combined lab-field studies, and investigating gene-environment interactions. We conclude with a discussion of acceptability, compliance, privacy, and ethical issues.

Keywords

ecological validity; smartphone; e-diary; psychophysiological monitoring; behavior observation

INTRODUCTION

Despite unparalleled advances in technology over the past several decades, the clinical assessment of psychopathology and psychological problems, as typically practiced, still relies on traditional paper-and-pencil questionnaires and face-to-face clinical interviews. However, these tried-and true methods are limited in a number of ways, including total reliance on patients' retrospective self-report, the skill of the clinical interviewer, and the artificial setting of the assessment (the clinic). In this review, we define and discuss a burgeoning research approach that promises to overcome many of the limitations of traditional clinical assessment approaches while providing rich information about the daily

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lives of individuals who may be studied or treated by clinical scientists and mental health professionals.

WHAT IS AMBULATORY ASSESSMENT?

Ambulatory assessment (AA) is an important research tool that has come into its own over the past two decades, promising to minimize retrospective biases while gathering ecologically valid data, including self-reports, physiological or biological data, and observed behavior, for example, from daily life experiences. Recently, P. Wilhelm et al. (2011) provided a historical overview of daily life research, explaining the factors that led to the development of the AA approach. But before launching into a discussion of the philosophy behind AA and providing examples of its use in clinical assessment and in intervention, it is important to provide a definition of AA and to outline its relationship to other forms of experience sampling.

AA uses a wide range of assessment methods to study people in their natural environment, including self-report, observational, and biological/physiological/behavioral. Here, we use the term AA to represent a methodological umbrella that encompasses increasingly computerized or digitized methods of experience sampling (historically using paper-and-pencil diaries), ecological momentary assessment (typically using electronic diaries or mobile phones), and continuous psychophysiological, biological, and behavior monitoring (typically using sensors or actigraphs). Although some use the terms AA, ecological momentary assessment (Stone & Shiffman 1994), experience sampling method, ecological momentary intervention, real-time data capture, continuous unified electronic diary method (Ellis-Davies et al. 2012), and e-diary methods interchangeably, we adopt the term AA because it captures the wide variety of methods, sampling, and data structures involved in the assessment of daily life experience (Fahrenberg & Myrtek 2001, P. Wilhelm et al. 2011; http://www.ambulatory-assessment.org).

Many features distinctly characterize AA from more traditional assessment approaches. AA (*a*) is idiographic in focus and allows for the examination of multiple individual processes (emotional, behavioral, psychophysiological); (*b*) is characterized by the collection of data in real-world environments, increasing the ecological validity of findings; (*c*) focuses on individuals' current or very recent states or behaviors and collects multiple assessments of each individual over time, typically several times per day; and (*d*) can be continuous (in the case of physiological assessment, for example), event based (initiated by the individual based on instructions), interactive (initiated by physiological signals detected by monitoring devices), time based, or randomly prompted (as well as combinations of these).

AA has many conceptual advantages over traditional research designs when investigators are interested in characterizing dynamic, clinically important psychological processes. Relative to laboratory research, AA has the advantage of being ecological—processes such as mood can be studied in participants' "natural habitats," where they are subject to the many environmental and interpersonal factors that typify their lives but cannot be recreated in the laboratory. Of course, AA research can sample not only the process of interest (e.g., mood, alcohol use) but also characteristics of the environment (e.g., location, time of day,

presence of interpersonal conflict) that change over time and may be important in explaining variation in the process of interest. Thus, AA studies can yield exceptionally rich descriptive data.

Another advantage of AA studies is that they are designed to capture momentary ratings. Historically, investigators have often attempted to gather data on dynamic psychological processes by using single-occasion retrospective self-reports. Although, intuitively, the argument for obtaining data on persons in real time or near real time is compelling, it is important that momentary assessments in the real world are shown to provide some incremental validity over both retrospective and dispositional reports of the individual. In other words, does the cost-benefit ratio favor momentary reports like those afforded through AA? It has been shown that the accuracy of these momentary reports is higher than retrospective reports of events, behaviors, and experiences (e.g., Schwarz 2011, Solhan et al. 2009). Furthermore, if the goal is to assess biological, psychological, or behavioral processes, then it is clear that multiple assessments over relevant time periods are necessary, as opposed to cross-sectional or global reports. Beyond these clear advantages of AA over retrospective and global reports, it seems likely that AA data are uniquely qualified to define and conceptualize the “experiencing self,” which can then in turn be linked to autonomic and biological systems (Conner & Barrett 2012). Therefore, if the goal is to identify biological and physiological features or systems that are associated with one’s immediate experience, AA provides measurement most proximal in time to the biological and physiological underpinnings of experience in the real world.

Computerization represents another advantage of AA protocols over traditional field techniques. Investigators have often collected field data using paper diaries, asking individuals to complete one or more diary entries per day between visits to the study center. A chief limitation of this approach is that investigators cannot be sure that the ratings were actually completed at the times specified by the research design. Participants may neglect making scheduled ratings, then backfill their diaries before reporting to the study center to avoid admitting they failed to make the scheduled ratings (Stone et al. 2002). AA studies using computerized or digital devices eliminate this problem because electronic devices [e.g., personal digital assistants (PDAs), smartphones] time stamp both prompts and entries. Furthermore, participants using electronic devices typically show high rates of compliance at the time of the scheduled prompt. For example, subjects drawn from a variety of clinical populations have provided timely responses to 85% or more of the delivered prompts (Collins et al. 1998, Hufford et al. 2002, Shiffman et al. 1996, Stone & Shiffman 2002, Trull et al. 2008).

Before discussing the methods and uses of AA in more detail, we want to highlight many excellent reviews and resources related to AA of clinical problems that have appeared recently. For example, a special section on AA approaches appeared in *Psychological Assessment* in 2009 (Trull & Ebner-Priemer 2009), including articles focused on substance use disorders (Shiffman 2009), anxiety disorders (Alpers 2009), mood disorders and mood dysregulation (Ebner-Priemer & Trull 2009), and psychosis (Oorschot et al. 2009). Haedt-Matt & Keel (2011) provided a meta-analysis of studies using AA to address the affect regulation model of binge eating. Telford et al. (2012) reviewed a number of AA studies that

address various aspects of the etiology and maintenance of depression, as have Aan Het Rot et al. (2012), Myin-Germeys et al (2009), and Wenze & Miller (2010). Both Nica & Links (2009) as well as Santangelo et al. (2012) reviewed AA studies of borderline personality disorder (BPD). Special sections on AA methods appeared recently in *Psychosomatic Medicine* (Kubiak & Stone 2012) and in *Schizophrenia Bulletin* (Ben-Zeev 2012). Finally, we point readers to several recent books that provide a range of coverage on the conceptualization, implementation, and analysis of data from AA studies (Mehl & Conner 2011, Stone et al. 2007).

Our article does not attempt to comprehensively review studies using AA, given these recent reviews targeting specific clinical disorders and methods. Furthermore, we focus primarily on clinical problems other than substance use disorders, given Shiffman et al.'s (2008) previous contribution to the *Annual Review of Clinical Psychology* that used many studies of these disorders as exemplars (especially tobacco dependence).

Methods of Ambulatory Assessment

A wide range of AA methods exist. Here, we organize these into three categories: self-report, observational, and physiological/biological/behavioral.

Self-report AA—This form of AA is probably the most familiar. Here, individuals provide responses to queries that are either prompted (e.g., random prompts or prompts at set times) or self-initiated (e.g., when a predefined event occurs such as drinking alcohol, having an interpersonal encounter, craving a substance, etc.). Questions, response formats and time-frames, and sampling schedules vary depending on the research question or the clinical construct being addressed (Ebner-Priemer & Sawitzki 2007, Palmier-Claus et al. 2011). Conner & Lehman (2011) provide practical guidelines for choosing the appropriate length of monitoring as well as the frequency of assessments per day, given the target constructs and the research question.

Many devices are used to collect AA self-reports. In early AA research, PDAs and interactive voice response (IVR) systems were used. In both cases, individuals responded to queries (either written text in the case of PDAs or voice in the case of IVRs) by selecting response options using a stylus or pressing buttons. Although both technologies are serviceable, they have been largely supplanted by mobile phones and by smartphones. In the case of mobile phones, text messaging is frequently used to contact individuals and to gather data. Smartphones can accommodate many more types of self-reported data collection, including text messaging, responses to survey questions presented on screens, voice recordings/dictation, and video logs, to name some of the possibilities.

There are many advantages to obtaining self-reports through AA, and most studies include this mode of assessment. However, it is important to recognize some limitations and caveats. A concern with all self-report assessments is whether memory heuristics or biases may influence the validity of the results. This is perhaps less a concern for AA self-reports because they typically concern immediate or very recent mood, thoughts, and behavior. Furthermore, it seems probable that AA self-reports, given that they characterize the immediate, experiencing self, are most likely to be associated with physiological and

biological processes of these reported states as opposed to retrospective or trait self-reports (Conner & Barrett 2012).

Perhaps a larger concern for AA self-reports is that of reactivity (Barta et al. 2011). Studies have documented the reactivity of traditional self-monitoring in terms of ultimately changing the frequency of the behavior one is monitoring (e.g., drinking, smoking). However, are AA self-reports vulnerable to reactivity effects as well? Barta et al. (2011) note that although, in general, it seems AA self-reports are not likely to be affected greatly by reactivity, some studies do show such an effect. For example, Conner & Reid (2012) demonstrated reactivity effects on the reporting of mood using mobile technology, and recently Courvoisier et al. (2012) reported evidence for reactivity (a time-dependent compliance pattern) as well.

So, how might one detect or protect against reactivity in AA? In order to address the possibility of reactivity in AA research, Barta et al. (2011) suggest using appropriate control groups (e.g., a group that does not use AA diaries), examining the data for any trends or response changes that may suggest reactivity effects (both within and across participants), looking for evidence of response shifts where participants may change the meaning they assign to scale ratings, and ensuring that data are as likely to be contributed on certain days (e.g., weekend days) or times of day (e.g., late evening) that might be associated with the behavior of interest (e.g., drinking alcohol). Large studies with thousands of participants allow investigators to integrate control groups with a small number of e-diary questions into the overall study so that one can calculate study-specific reactivity.

Finally, there is the concern about the generalizability of AA self-report data: Perhaps certain individuals are deterred from participation because of the perceived complexity of the technology (hardware and software) such that only the most motivated and those most open to new technology may take part (Palmier-Claus et al. 2011). In our experience, many researchers and clinicians remain skeptical about the ability or willingness of patients with severe disorders to comply with AA research protocols. However, this apprehension seems largely unfounded (Ben-Zeev 2012, Wenze & Miller 2010). To the contrary, even severely ill patients (e.g., with schizophrenia, BPD, or substance dependence) show good compliance and low dropout rates in general. Furthermore, these patients do not appear to be censoring reports, often endorsing dysfunctional or less socially desirable behaviors such as cutting, drinking, and bingeing.

Observational AA—Perhaps less familiar are observation methods of AA. These do not rely on the self-report of the individual and provide a means for assessing ambient sound, speech, activity, location, and context. For example, the Electronically Activated Recorder (EAR; Mehl & Robbins 2011) is an audio-recording device worn by individuals that periodically samples short segments of ambient sounds (including conversations) in the environment. In providing an observer's point of view rather than the typical agent's point of view, the EAR is a methodological tool that has the potential to offer unique information in the assessment of behavior (Mehl & Robbins 2011). Like other forms of AA, the EAR maintains ecological validity by recording participants in their natural environment and by allowing for intensive longitudinal assessments. Also, as an observational alternative to self-

report, the EAR has the potential to provide information that participants may be unable or unlikely to report due to limitations in self-awareness, poor recall of events, social desirability biases, and the inability to aggregate information (Wilson & Dunn 2004). Although the EAR is limited in that it can assess only audible traces of behavior and affect, it bypasses many of the problems associated with traditional observational methods. Most EAR data are still coded by trained raters, but automated systems to classify emotions and affect in speech are available (Rachuri et al. 2010, Schuller et al. 2011).

Recently, Tomko et al. (2012) used the EAR to assess interpersonal behavior and affect in patients with BPD and patients with current depressive disorder. The EAR was worn by these patients for three consecutive days and periodically recorded 50-second snippets of ambient sounds. Trained coders listened to the captured recordings and rated participants' affect during each 50-second clip (i.e., in naturally varying social contexts). Results indicated that depressed patients were less likely to spend time with others when experiencing anger than were BPD patients. Furthermore, there were differences between diagnostic groups regarding the social context of anger, such that anger at a previous time interval predicted spending time alone in the subsequent time interval for the depressed group, but not for the BPD group.

Other forms of AA observational methods include collecting global positioning system (GPS) data from sensors in phones or devices on the person, using light sensors to infer context (e.g., inside versus outdoors), using still photos or video cameras to record surroundings/context, and using video or sensors to detect interaction with other people. For example, Vahabzadeh et al. (2010) reported on an ongoing study in which treatment-seeking drug-dependent patients carry an electronic diary and a GPS logger for many weeks, such that their activities and locations could be assessed. What is unique about this study is that the urban area the patients inhabit has been geocoded for "environmental disarray," which includes scores related to likelihood of crime, drug use, and drug dealing, among other features. Therefore, integrating electronic diary and GPS data will allow investigators to examine environmental influences on drug craving, drug buying, and relapse.

Although there are many advantages to observational AA (e.g., not relying on patient self-report, remaining relatively unobtrusive and therefore not as vulnerable to reactivity effects), there are limitations as well. First, many observational AA methods target only one form of activity or channel. For example, the EAR can only tell us about audible events, situations, or contexts. On the other hand, photos will not record acoustic information. Second, most observational AA devices still require the cooperation of participants; the devices must be worn as instructed. Finally, some of these devices have both power and storage limitations. These limitations may require participants to charge the devices often and to frequently come into the lab to download the stored data.

Physiological/biological/behavioral AA—As mentioned previously, many identify the term AA with ambulatory physiological or biological assessment, although AA is now much broader than assessment in these domains. A number of physiological and biological processes are associated with psychopathology, personality, and problematic emotions and behavior. Many studies have examined electro-dermal activity, cardiac activity and heart

rate variability, and respiration correlates of psychopathology. For example, Meuret et al. (2011) explored the physiological precursors to and correlates of unexpected panic attacks by conducting repeated 24-hour ambulatory monitoring of patients with panic disorder. Interestingly, the hour before the panic attack onset was characterized by variability in heart rate (rising and then dropping several cycles), instability in breathing rate, and higher levels of electro-dermal activity. In contrast, less change or variability in physiological activity was observed after panic onset and following the panic attack. These results suggest that patients did not perceive the physiological changes leading up to an unexpected panic attack and challenge the idea that physiological arousal or instability does not occur until the onset of unexpected panic attacks.

Another form of physiological/biological AA includes the assessment of hypothalamic-pituitary-adrenal axis activity by collecting salivary cortisol during daily life. Cortisol reactivity to stressful events is believed to be enhanced in those with emotion regulation problems. Havermans et al. (2011) explored whether cortisol reactivity patterns would differentiate remitted bipolar patients from normal controls. Patients in remission from bipolar disorder and healthy controls were prompted 10 times a day for six consecutive days to produce a saliva sample and, at each time point, were asked about the experience of a positive or a negative event since the last prompt. Results indicated that the two groups did not differ in mean cortisol levels over the six days and that members of both groups, on average, showed similar levels of cortisol reactivity to negative events. However, remitted patients showed less diurnal decrease in slope of cortisol level during the day as well as lower autocorrelation between successive cortisol levels than did the healthy control group. The latter finding indicates that cortisol secretion was less stable over successive measurements, suggesting that this may be a hypothalamic-pituitary-adrenal dysregulation marker among remitted bipolar patients.

Actigraphy is used in AA in order to quantify physical activity level. Three-axis accelerometers can be worn on the wrist or ankle in order to quantify activity level and to make inferences about type of activity based on body position and movement (e.g., walking, running, lying down). Many forms of psychopathology may be associated with activity level, for example, depression and reduced activity or mania and hyperactivity. Furthermore, it is important to take activity levels into account when interpreting AA physiological data because activity level can affect electro-dermal activity, cardiac activity, and respiration (Houtveen & de Geus 2009).

It may be helpful to illustrate the use of actigraphy in the study of psychopathology. For example, Aronen et al. (2011) were interested in motor retardation as a cardinal feature in depression. Objectively measured motor activity distinguished depressed children from their nondepressed peers, both during daytime and nighttime. In depressed children, motor activity was linked with the severity of self- and teacher-reported symptoms, as well as with suicidal ideation specifically. It is also worth noting that results for actigraphy studies have revealed discrepancies between objective assessments of physical activity and self-report, parent report, or expert report (Adamo et al. 2009, Bussmann & Ebner-Priemer 2011, Prince et al. 2008, Razavi et al. 2011). This is especially concerning in the area of child and youth clinical assessment for hyperactivity or physical aggression. These AA studies suggest that

subjective reports of activity level should be interpreted with caution. Finally, actigraphy studies have also been used to investigate the effects of medications on motor activity in mood disorders (Baune et al. 2007, Benedetti et al. 2007).

If researchers are interested in behavioral or physiological aspects of functioning, the objective measurement of these processes in everyday life using psychophysiological or behavioral AA is the gold standard (Adamo et al. 2009, Bussmann & Ebner-Priemer 2011, Prince et al. 2008). However, the costs of such studies are usually higher because of the expense of devices, the management of large amounts of data, and the complexity of data analyses. Additionally, the burden of the participants is higher, too, which explains why the duration of most AA physiological studies often is only 24 or 48 hours. Several recent publications offer good overviews of the devices, methods, empirical findings, and caveats in psychophysiological and behavioral monitoring (Bussmann & Ebner-Priemer 2011, Ebner-Priemer & Kubiak 2007, Houtveen & de Geus 2009, F.H. Wilhelm et al. 2011).

THE USE OF AMBULATORY ASSESSMENT IN CLINICAL PSYCHOLOGY

We now turn our attention to several topics related to the current use of AA in clinical psychology (*a*) to investigate mechanisms and dynamics of psychopathological symptoms, (*b*) to predict the future recurrence or onset of symptoms, (*c*) to monitor treatment effects, (*d*) to predict treatment success, (*e*) to prevent relapse, and (*f*) to administer interventions.

Investigating Mechanisms and Symptom Dynamics

The repeated nature of AA enables researchers to investigate how psychopathological symptoms are related to each other across time and environments, such that the dynamics and mechanisms of psychopathology can be explored in much more detail than was previously possible. To illustrate, we present several studies targeting major depressive disorder (MDD) and BPD.

Assessing putative mechanisms—AA can be used to investigate mechanisms believed to underlie significant emotional changes in everyday life. Here we summarize recent research on two potential mechanisms relevant to MDD: stress sensitivity and reward experience. Stress sensitivity can be defined as the experience of negative affect (NA) following negatively appraised daily life events. Reward experience can be defined as positive affect (PA) in response to positively appraised (i.e., pleasant) situations. This mechanism may help explain how positive emotional responses in daily life can decrease both stress sensitivity and the expression of genetic risk for depression (Wichers et al. 2010).

In an early study, Peeters et al. (2003) assessed stress reactivity and reward experience in patients with MDD and in healthy controls (HCs) using paper-and-pencil diaries. Surprisingly, in comparison with the HCs, MDD participants showed blunted NA responses to negative events (i.e., reduced stress reactivity) and enhanced PA responses to positive events (i.e., enhanced reward experience). Although their NA responses to negative events were blunted, NA responses to negative events persisted longer in MDD participants, and MDD participants reported fewer positive events. Finally, MDD participants with a positive family history for depression or with longer current depressive episodes showed relatively

greater NA responses to negative events. A later study that added more participants to this protocol showed increased stress reactivity in individuals with MDD compared to HCs (Myin-Germeys et al. 2003), and this finding was subsequently replicated by Wichers et al. (2009).

The heritability of these purported mechanisms was investigated in two studies. Wichers et al. (2007) showed that nondepressed twins with a cotwin diagnosed with MDD exhibited greater stress reactivity than did individuals with a healthy cotwin, suggesting that genetic liability to depression may, in part, be expressed by a heightened NA response to everyday stress. In addition, Wichers et al. (2009) investigated whether genes associated with depression may act by accelerating the process of stress sensitization following stress exposure over the life course. Indeed, nondepressed twins at high genetic risk for depression (i.e., with a cotwin with a history of depression) exhibited higher levels of daily life stress sensitivity as a function of exposure to both prenatal stress (low birth weight) and postnatal stress (childhood adversity and adult recent negative life events) than did those at low genetic risk. These findings suggest that, in MDD, high stress sensitivity in everyday life may be at least partially the result of an inherited vulnerability combined with acquired developmental challenges (e.g., childhood adversity).

These studies examining potential mechanisms of depression are promising, but it is important to recognize some of their limitations as well. In addition to problems in defining and operationalizing these mechanisms (e.g., how do you separate the effect of the event from the appraisal of the event in stress reactivity?), criticism has been raised regarding the simultaneous assessment of events, appraisal of events, and affect (Geschwind et al. 2010). Future research should attempt to disentangle these constructs, perhaps by separating questions for different domains (e.g., events, appraisals, and affects) into different assessments. Despite these limitations, we do see the assessment of putative mechanisms of depression and other forms of psychopathology as a very promising application within the AA field.

Assessing affective dynamics—Traditional clinical assessment approaches (e.g., cross-sectional assessment, retrospective assessment) cannot uncover and precisely characterize the ebb and flow of symptoms. Many disorders and symptoms are defined and characterized by instability, a feature that can be measured only by multiple and frequent assessments. For example, AA studies have demonstrated heightened affective instability in individuals with BPD compared to HCs (Ebner-Priemer et al. 2007) and compared to depressive patients (Trull et al. 2008). Highlighting the limitations of traditional assessment approaches, research has shown that the relationship between retrospective questionnaire trait measures of affective instability and affective instability as experienced in everyday life is modest at best (Links et al. 2003, Solhan et al. 2009). At the same time, it is important to acknowledge that the quantification and characterization of dynamic processes such as mood is challenging. Fortunately, a number of methodological papers have appeared in recent years, presenting multilevel models to analyze instability of symptoms (Eid et al. 2011, Jahng et al. 2008, Trull et al. 2008), investigating the appropriateness of time-based sampling designs (Ebner-Priemer & Sawitzki 2007), visualizing instability patterns (Ebner-

Priemer & Trull 2011), and analyzing multidimensional unstable processes (Ebner-Priemer et al. 2009).

Predicting Psychopathological Symptoms

Wichers et al. (2010) investigated the degree to which daily life (*a*) stress sensitivity, (*b*) reward experience, (*c*) fluctuations in NA and PA, and (*d*) mean NA and PA might improve the prediction of future recurrence of depressive symptomatology in remitted depressed subjects. Toward this end, they used paper-and-pencil diaries to assess women with a history of major depression over five consecutive days. Diaries were used to document mood, stress sensitivity, and reward experience. Depressive symptomatology was assessed at follow-up several times up to 14 months later. Wichers et al. (2010) found that reward experience and daily life fluctuations in NA significantly predicted future negative affective symptoms over and above what could be predicted by questionnaires. Mean NA and reward experience were the strongest predictors for recurrence of MDD.

Geschwind et al. (2010) examined prospectively whether high reward experience protects against negative affective symptoms (anxiety, depression) and whether environmental or genetic risk factors moderate these protective effects. Approximately 500 female twins participated in an experience sampling study measuring reward experience in daily life. They also completed questionnaires targeting childhood adversity and recent stressful life events. Negative affective symptoms were measured at baseline and at four follow-ups using questionnaire anxiety and depression subscale scores. Co-twin negative affective symptoms were used as indicators of genetic risk. Findings revealed no overall association between reward experience in daily life and later affective symptoms, regardless of level of genetic risk. However, lower reward experience predicted later affective symptoms, when controlling for baseline affective symptoms, in people with a history of childhood adversity or recent stressful life events.

Monitoring Treatment Effects

Perhaps the earliest study reporting monitoring of treatment using AA was conducted by Klosko et al. (1990), who used daily self-monitoring to track panic episodes during a medication trial. Five years later, Barge-Schaapveld et al. (1995) evaluated the effects of antidepressants in MDD patients, assessing patients using paper-and-pencil diaries before and after six weeks of treatment. Compared to nonresponders, treatment responders showed greater increases in positive affect and greater decreases in negative affect during all activities as well as greater increases in time spent on chores and greater decreases in passive leisure time.

In a second clinical drug trial, Barge-Schaapveld and colleagues (Barge-Schaapveld & Nicolson 2002, Wichers et al. 2009) used paper-and-pencil diary assessment in patients with current MDD and HCs to investigate the effects of six weeks of either imipramine or placebo. Barge-Schaapveld & Nicolson (2002) used quality of life as an outcome measure. Despite greater clinical improvement in depression at week six, participants receiving antidepressants did not report greater increases in momentary quality-of-life ratings compared to participants receiving placebo. By week 18, although remitted participants'

global quality of life improved (as measured by retrospective questionnaires), the momentary assessments of patients' quality of life suggested less improvement. Using the same data set, Wichers et al. (2009) found that momentary stress sensitivity and reward experience changed in the same direction in the placebo group and the antidepressant group. However, stronger effects were found in the active treatment group. Additionally, increase in reward experience discriminated between treatment responders and nonresponders.

Finally, Geschwind et al. (2011b) recently investigated the effects of mindfulness-based cognitive therapy on momentary positive emotions and on the ability to make use of natural rewards in daily life. Study participants had residual depressive symptoms and a lifetime history of depression, and they were randomized to a mindfulness-based cognitive therapy group or to a wait-list group. Paper-and-pencil diaries were used to assess PA, NA, and the appraisal of pleasant activities in daily life during the six days before and after the intervention. Compared to the control group, patients receiving mindfulness-based cognitive therapy rated their current activities as increasingly pleasant, their PA levels increased, and their NA levels decreased. The treatment group also showed an increase in reward experience. This effect was independent of depressive symptoms, rumination, and worry. Given the role of positive emotions in resilience against depression, it appears reward experience may contribute to the protective effects of mindfulness-based cognitive therapy against depressive relapse (Geschwind et al. 2011b).

Predicting Treatment Success

Geschwind et al. (2011a) provided impressive support that early improvement in positive rather than negative emotions best predicted success in pharmacotherapy. Participants with depression took part in two experience-sampling periods: during an initial baseline week and during the last three days of the first week of treatment with medication. Early improvements in PA during the first week of treatment, compared to the baseline week before, significantly predicted continuous depressive symptomatology as well as response and remission, independent of change in NA. Early improvement of PA was associated with a 34 times higher chance of achieving remission. Furthermore, all participants with early improvement of PA qualified as a treatment responder at week six. The authors suggested that antidepressants might activate resilience-like mechanisms and that monitoring of positive emotions in early stages of treatment may improve clinical decision making.

Peeters et al. (2010) and Wichers et al. (2012) used AA indices of emotional reactivity to predict improvement and remission in major depression. In the Peeters et al. (2010) study, MDD patients received pharmacotherapy with supportive psychotherapy and were followed and assessed for response status and depression level over the next 18 months. Paper-and-pencil diaries were used to assess affect and appraisals for six days before start of treatment. Individuals who exhibited reduced NA reactivity to negative life events were less likely to remit from MDD over the 18-month follow-up period, even after controlling for initial depression severity, episode duration, and baseline mean mood levels. In addition, diminished reactivity to everyday life events predicted relatively higher depression severity levels during the first month of the follow-up period, over and above what could be accounted for by baseline depression severity, episode duration, and mean levels of reported

mood. However, diminished emotional reactivity only predicted depressive symptoms at the earliest follow-up points and did not predict symptoms at subsequent follow-up points (2 months, 3 months, 6 months, 12 months, and 18 months).

Wichers et al. (2011) found that a reduction in NA following the maximum increase in PA provided a means to discriminate between treatment responders and nonresponders, and higher NA after the maximum PA increase was associated with more depressive symptomatology at six-month follow-up. No significant differences were found for any other type of NA-PA dynamic. Whereas retrospective measures of depressive symptomatology at baseline had no predictive value regarding outcome, dynamic daily life patterns of negative and positive emotions showed incremental predictive validity. A more favorable future course of depression was associated with stronger reductions of NA following increase in PA over the course of the day.

Most recently, Forbes et al. (2012) sought to predict the course and outcome of an eight-week open trial of cognitive behavioral therapy (CBT), pharmacotherapy, or a combination of the two in children and adolescents with depressive and anxiety disorders. Given that adolescents with depression report experiencing heightened sensitivity to social rejection and increasing symptoms during isolation from peer cliques, Forbes et al. (2012) also assessed social dynamics (with companions) using e-diaries in natural settings over the four days before treatment. Higher PA, lower NA, a higher PA:NA ratio and more time spent with fathers predicted lower posttreatment severity, depressive symptoms, and anxiety symptoms. Furthermore, Forbes et al. (2012) examined the predictive validity of momentary affect above and beyond retrospective self-reports of depressive and anxiety symptoms. Retrospective self-reports did not predict the course of clinical severity over treatment, whereas NA did, indicating added value for AA.

Relapse Prevention

Because many psychiatric disorders are episodic in nature, relapse prediction and prevention programs are of major interest. AA devices such as smartphones can be used to monitor symptoms in real time, calculate risk for new episodes of illness on an individual basis, and even administer therapeutic interventions. Spaniel et al. (2008a) developed a relapse prediction and prevention program for schizophrenia to identify prodromal symptoms of relapse in schizophrenia, to enable early intervention, and to prevent unnecessary hospitalizations. In a one-year open trial, patients with schizophrenia and their family members were sent a 10-item questionnaire weekly about early warning signs of schizophrenia via short message service (SMS; texting). Responses were returned via SMS, and if the total score of the responses exceeded a given threshold, an early intervention process was triggered: (*a*) The psychiatrist was notified by an email message and encouraged to contact the patient by phone, (*b*) the dose of antipsychotic medication was increased by 20% within the next 24 hours, and (*c*) the SMS questionnaire prompts to family members were doubled. The researchers reported a 60% reduction in the number of hospitalizations compared to the one-year period prior to the intervention. Although these results are promising, the study did not include a control condition to rule out alternative explanations. In a one-year extension of this study including additional patients with

psychotic illness, Spaniel et al. (2008b) confirmed their main findings, reporting a 77% decrease in the number of hospitalizations and a 60% decrease in the number of hospitalization days.

Interactive Ambulatory Assessment: Interventions in the Real World

There are a number of compelling arguments for AA as an intervention platform (Clough & Casey 2011, Cohn et al 2011, Depp et al. 2010, Ebner-Priemer & Trull 2009, Wichers et al. 2011). First, for decades, clinicians have struggled with the challenge to translate principles and strategies learned in the clinician's office to the real world of the patients. AA can enhance the transfer of skills to real-world settings by prompting individuals to apply their skills in daily life, when and where they are needed. Second, AA methods foster engagement and adherence. For example, Clough & Casey (2011) suggest that many clients maintain a personal relationship with their mobile devices, as these devices provide a direct link to their social and support networks. Clients typically carry their mobile phones on their person throughout the day, and the widespread use of smartphones also reduces the chance of feeling embarrassed about completing diaries in public. Third, self-monitoring greatly facilitates self-management (Wichers et al. 2011). For example, quantifying and depicting patterns of daily life emotional experience may give patients insight into the nature of their own depressive symptomatology. Finally, even though mental health treatment has become much more affordable in the past 20 years, many patients are still not adequately treated for financial reasons. Interventions using the AA platform can be a more cost-effective approach, reducing the frequency of face-to-face sessions or even replacing the need for in-person psychosocial intervention altogether.

The use of the AA platform to administer empirically supported treatments is still in its infancy. A recent review on AA interventions for smoking cessation, weight loss, anxiety, diabetes management, eating disorders, alcohol use, and healthy eating and physical activity can be found in Heron & Smyth (2010). Here we present a few examples.

AA intervention for anxiety disorders—The most extensive body of studies investigating the use of the AA platform for treatment has targeted anxiety disorders. In a series of studies, a palmtop computer–assisted treatment program for anxiety disorders was tested and evaluated. The palmtop computer beeped several times per day, prompting patients to self-monitor their anxiety levels and to practice techniques in response to anxiety cues. The palmtop computer administered the following treatment modules: self-statements, breathing control, situational exposure, and interoceptive exposure. In an early uncontrolled pilot study, Newman et al. (1997) attempted to improve the efficiency and cost-effectiveness of CBT by using adjunct palmtop computer–assisted therapy. The researchers randomly assigned patients to a 12-session CBT condition or to a four-session computer-assisted CBT condition. Results indicated improvements in both treatment conditions over time and no differences between groups, suggesting that both treatments were equally effective at posttreatment and at six-month follow-up. The palmtop computer–assisted treatment program has also been used in single cases with generalized anxiety disorder (Newman et al. 1999) and social phobia (Przeworski & Newman 2004). When the authors examined

treatment costs, they estimated a savings of $540 to $630 per client when compared with standard individual CBT (Newman et al. 1997, 1999).

In a subsequent study, Kenardy et al. (2003) compared a 12-session therapist-delivered CBT treatment, a brief six-session therapist-delivered CBT treatment, a palmtop computer–augmented six-session therapist-delivered CBT treatment, and a wait-list condition. Approximately 200 patients with panic disorder across two sites in Scotland and Australia were randomly assigned to treatment conditions. Patients in all treatment conditions showed improvement compared to the wait-list group at posttreatment. At posttreatment, the 12-sessionCBTcondition showed stronger effects compared to the six-session CBT without the computer. The overall effect of the palmtop computer–augmented treatment fell between the other two treatment conditions and could not be statistically distinguished from either one. There were no differences between the active treatment conditions at six-month follow-up. Treatment costs were lower for the brief treatment and for the computer-augmented condition compared to the standard treatment.

Gruber et al. (2001) used palmtop computers as an adjunct to cognitive behavioral group therapy for social phobia. Patients were randomly assigned to a 12-session cognitive behavior group therapy, to an eight-session cognitive behavioral group therapy utilizing handheld computers to facilitate homework assignments, or to a wait-list control group. At posttreatment, both treatments were superior to the wait-list control on most behavioral measures, but the computer-assisted therapy and the wait-list conditions did not differ significantly on self-report measures. At posttreatment and follow-up, standard therapy and the brief computer-assisted therapy were equally effective in reducing symptoms and improving behaviors associated with social phobia.

AA intervention to remind clients to use previously learned skills—Norton et al. (2003) described the development of an integrative cognitive therapy for eating disorders including palmtop modules as therapy extension devices. Similarly, Solzbacher et al. (2007) discussed the development and application of a distress regulation reminder sent via cellular phone during high levels of distress in those with chronic posttraumatic stress disorder, bulimia nervosa, and BPD. Kimhy & Corcoran (2008) presented a case report of using AA as a treatment adjunct to improve homework completion and overcome treatment barriers associated with negative symptoms with a female patient at high risk for psychosis. Finally, Depp et al. (2010) recently reported on a pilot study where outpatients with bipolar disorder received a preselected self-management strategy reminder after signaling to the PDA that they were experiencing an exacerbation in symptoms or an episode trigger.

AA intervention using text messaging—An intervention using text messaging on mobile phones in the psychological aftercare of patients suffering from bulimia nervosa was developed by Bauer and colleagues (Bauer et al. 2003, Robinson et al. 2006, Shapiro et al. 2010). Bauer et al. (2003) investigated SMS text messaging in the aftercare of patients suffering from bulimia nervosa. Participants were required to report weekly on their symptoms, and the researchers replied, offering support and advice. The program lasted six months following inpatient treatment and aimed to reduce the risk of relapse. Reporting on

two patients, Bauer et al. (2003) suggested that the SMS aftercare intervention was a helpful bridge between inpatient treatment and outpatient daily life.

Robinson et al. (2006) used this same approach in patients with bulimia nervosa, starting directly after outpatient treatment. Although similar software and methodology were used, Robinson et al. reported low usage and high attrition rates, and found only small effect sizes for improvement. Less than half of participants completed the study. Most participants viewed the lack of personal contact negatively and indicated that they would not recommend the program to others. The authors noted that the SMS program was a minimal aftercare intervention, which may not have been appropriate for the more severe cases. Shapiro et al. (2010) recently reported a feasibility study using the same SMS text-messaging approach during a 12-week outpatient CBT treatment group program for bulimia nervosa. Again dropout rates were high (between 50% and 60%, depending on how dropout was calculated). Four questions were administered at the end of the day, followed by an individualized feedback message. Additional symptoms were assessed using daily paper-and-pencil diaries.

On the more positive side, Granholm et al. (2012) developed an interactive text-messaging intervention for patients with schizophrenia. SMS messages focused on medication adherence, socialization, and the experience of auditory hallucinations. These text messages were sent to participants with schizophrenia three times daily for a 12-week period. Participants first received two assessment text messages regarding psychopathology as well as cognitions. In addition, patients completed two assessments following the texted personalized interventions, including, for example, thought-challenging messages for unhelpful beliefs or behavioral coping or behavioral experiment suggestions. In addition, the participants received weekly summarized feedback. The authors reported a dropout rate of 24%, much higher than in regular AA studies, but similar to that of AA treatment studies (e.g., Solzbacher et al. 2007). Granholm et al. (2012) reported improvements in medication adherence, socialization, and auditory hallucinations due to the intervention, but no control group was included, limiting the conclusions that can be drawn.

It is important to acknowledge some potential limitations in the SMS or texting approach to AA interventions. First, depending on the nature of the text message (i.e., texting questions directly versus texting a secure web page with questions and structured response formats), there may be limited response options available to the recipient. Furthermore, it may be cumbersome to use texting when there are many items in the survey, and it may be difficult to assess multiple symptoms via SMS. Another problem in using SMS as an intervention platform is the time delay of SMS messages sent. Contrary to patients' (and clinicians') expectations, not all SMS messages reach recipients in less than one second. Based on our own experience, in rare cases SMS messages may take up to an hour to be sent and received. This is especially problematic if the research design works with a sequence of SMS messages or if the timing of responses to the messages or of interventions is crucial.

Interventions using apps—Given the large number of consumer electronic applications (apps) that are available for tracking behaviors, habits, and symptoms, it seems clear that people have a great interest in monitoring and improving their symptoms. Increasingly, apps can be used to either enhance or administer mental health treatment. For example, Rizvi et

al. (2011) developed the DBT Coach, an interactive mobile phone application offering in vivo skills coaching for enhancing generalization of a specific dialectical behavior therapy (DBT) skill, as well as for reducing maladaptive urges and dysfunctional behavior in individuals with BPD. Individuals with BPD and comorbid substance use disorder who were enrolled in a DBT treatment program used the phone application for 10 to 14 days. Both emotion intensity and urges to use substances significantly decreased, reinforcing the idea that offering in vivo skills coaching may be a powerful tool for reducing maladaptive urges and dysfunctional behavior in individuals with BPD.

Luxton et al. (2011) recently conducted a search for all apps specifically developed for health and mental health issues. They discovered hundreds of apps, covering a wide range of relevant health topics including anxiety, depression, smoking, alcohol use, psychosis, diet, exercise, weight loss, nutrition, parenting, cognitive performance, relationships, relaxation, sleep, spirituality, and general well-being. According to Luxton et al. (2011), however, no oversight or standards for behavioral health via smartphone and associated apps exist. However, the U.S. Food and Drug Administration is working on regulations for mobile medical applications, and there is now published draft guidance for the industry to facilitate discourse (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM263366.pdf).

Our own review of health-related apps for electronic devices suggests that although some appear to be based on existing, empirically supported treatments or assessments, there is little evidence to indicate that these approaches have been validated or evaluated for use in an app format. There are also many apps that do not appear to be based on empirically supported treatments or assessments. Although studies that have directly and empirically evaluated the efficacy or effectiveness of apps targeting mental health constructs are scant, some of these initial efforts are clearly worthwhile and laudatory, given the seriousness of the problems they seek to address (e.g., the suite of posttraumatic stress disorder apps created by the U.S. Department of Veterans Affairs National Center for PTSD and the Department of Defense National Center for Telehealth and Technology).

Privacy concerns are of particular importance when evaluating the mental health–related apps that are currently available. Patient data entered into the app are often owned by the software company, which retains the right for use of the data. Even worse, Thurm & Kane (2010) reported that 55% of the apps tested in their study were found to send some of this information to other companies (i.e., other than the maker of the app). This is a significant risk to user confidentiality, especially when considering the target behaviors of many apps (e.g., smoking, alcohol use, psychosis, and weight loss). Clinicians, patients, and consumers should be aware of what information each app collects in order to make an informed choice regarding risk to privacy.

AA interventions to provide feedback or to administer novel treatment—Grassi et al. (2007) examined the use of mobile phones to deliver relaxation exercises in a sample of nonclinical participants. The software program was based on the principles of progressive muscle relaxation and other relaxation techniques. Interestingly, the program included audio- and video components to facilitate imagination of calm environments. Results

indicated that participants in a combined audio- and video-component group experienced significant reductions in anxiety as well as improvements in self-efficacy, with medium-to-strong effect sizes. No differences were found among other groups. Similarly, Morris et al. (2010) conducted a pilot test of ten subjects over a one-month period using a mobile phone application with surveys for mood reporting and as well as for administering treatment, including modules of breathing visualization, a physical relaxation animation, and a series of cognitive reappraisal exercises. The authors analyzed single cases and reported symptom reduction in some participants. Unfortunately, no control group or control condition was part of the study.

Tryon et al. (2006) used a sophisticated actigraphy device in boys with diagnoses of attention deficit-hyperactivity disorder. The device continuously measured physical activity during school periods. Individually tailored, moment-specific feedback, triggered by physical activity, was given to each boy in order to reinforce activity level reductions. Most of the participants greatly reduced their activity level (i.e., by 20% to 47% of baseline level). Whereas this approach is similar to laboratory-based biofeedback approaches, it differs essentially in that behavior was assessed and changed in the boys' natural environment.

Sorbi et al. (2007) developed a system called ODA (online digital assistance) that combines AA and online coaching. Direct feedback through the Internet was used to reinforce self-care and healthy behavior in everyday life. An initial study tested ODA's feasibility and acceptability in patients with migraine attacks. Participants were prompted several times a day by a PDA that was connected by a secure central server. Participants were questioned about migraine attacks and precursors of a migraine as well as preventive action. The answers were analyzed by the server, which calculated the current risk for a migraine attack using predefined algorithms. The participants received nearly immediate feedback about their current state, advice regarding how to circumvent migraine attacks (individually tailored to their current state), and "cheer ups" to enhance compliance and motivation.

Finally, Wichers et al. (2011) recently introduced a promising hardware device (PsyMate) for AA. It is designed to be used in standard clinical care for enhancing self-management by giving patients a visualization of their symptoms and their symptoms' context dependency. This feedback is thought to actively engage patients in the process of recovery and increase the patient's insight into the nature of the emotional dysregulation. In addition, clinicians using this device in their practice might get a better understanding of the nature of the individual's depression and increased insight in how medication impacts daily life mood states in the individual, and this information may better guide decisions on medication type or dosage.

THE FUTURE OF AMBULATORY ASSESSMENT IN CLINICAL PSYCHOLOGY

In this final section, we present and discuss several issues we believe will be most pressing and compelling in the development of future AA applications in the field of clinical psychology.

The Smartphone

A recent Pew survey indicated that 46% of American adults now own a smartphone, up from 35% a year earlier (Smith 2012). Worldwide, it is predicted that by 2014 there will be about 1.8 billion smartphone users (Portio Res. 2012). The most basic application of a smartphone is to prompt and log self-reported momentary responses in AA. However, the contemporary smartphone is much more than a PDA or a mobile phone. Today's state-of-the-art smartphone is actually a versatile computer that you just happen to talk with, possessing many positive features, including powerful processing capacity, large memory storage capacity, the ability to multitask, a range of connectivity possibilities with other devices, many built-in sensors (e.g., light sensors, proximity sensors, three-axis accelerometers, three-axis gyroscopes, Bluetooth sensors), the potential to link with external sensors (e.g., electro-dermal activity, cardiac activity, brain activity), GPS capabilities to track location and time, digital cameras and video recorders, and audio input/output and recording (Miller 2012).

With its onboard sensors and the capability to communicate and interact with other devices, the smartphone has become the central hub for AA. Here we present a sample of smartphone-based studies to illustrate the new possibilities.

Dufau et al. (2011) argue that studies investigating human cognitive faculties show limitations and sampling biases because of the use of small and homogeneous groups as volunteers coming to research facilities. They propose that smartphone technology can overcome this problem by collecting data in cognitive science experiments from thousands of subjects from all over the world. To demonstrate their point, they chose the lexical decision task, a psycholinguistic task where response time and accuracy is assessed while participants are engaged in deciding whether or not a letter string is a word. The task was programmed as an app for the iPhone and uploaded at the iTunes app store. Participants downloaded the app, performed one or more sessions of 50 to 140 randomly selected stimuli, and voluntarily provided data such as age, gender, handedness, and native language. Within four months the researchers received test results from more than 4,000 participants from all over the world, covering seven languages. Data showed the expected response distributions compared to laboratory data. In addition, a striking linear relationship between iPhone response and a within-laboratory lexical decision experiment was shown. It is also noteworthy that Dufau et al. (2011) argued that this AA methodology helped them sample a more diverse population than is typically represented in psycholinguistic experiments, namely undergraduate students. A similar approach has been used by Killingsworth & Gilbert (2010) to collect data on the relation between mind wandering and happiness in more than 5,000 participants using an iPhone app (http://www.trackyourhappiness.org).

Automatic recognition of emotion from speech is an emerging field of research in computer science (Schuller et al. 2011). Most of the work in emotion recognition is laboratory based. A noteworthy exception is a study by Rachuri et al. (2010), who developed EmotionSense, a smartphone-based fully context-aware programmable mobile sensing system. The system monitors audio signals, acceleration, Bluetooth signals, and location (GPS), and it is composed of a speaker-recognition subsystem and an emotion-recognition subsystem. Audio samples are recorded and processed to extract speaker and emotion information by

comparing it to a set of speaker-dependent models and preloaded emotions, installed during the setup phase of the system. The authors evaluated the system both in the lab with data from an emotion speech library and in everyday life. In the field study, participants gave additional information via e-diary about emotions, location, and presence of other people.

Smartphones are likely to play an even greater role in observational AA. These devices can record sound, take pictures, provide GPS data, and provide video recordings. Smartphones offer additional possibilities, including monitoring communication patterns by tracking application usage (Shepard et al. 2011) or tracking social context by assessing the density of local Bluetooth devices (Do et al. 2011). In a series of studies, Shepard et al. (2011) demonstrated that smartphone usage is person-specific and context dependent, meaning that different applications are used at different locations and different websites are visited at different times of the day. Person-specific usage patterns may be particularly informative because changes in communication behavior might be related to changes in mood. To monitor a range of processes on smartphones, Aharony et al. (2011) developed funf, an extensible sensing and data-processing framework for Android-based mobile devices. Funf provides an open-source, reusable set of functionalities, enabling the collection, uploading, and configuration of a wide range of data types, including scripts for data visualization.

Ecological Validity of Laboratory Results: From the Scanner into the Wild

A relatively untapped application of AA is to evaluate the ecological validity of laboratory results (Wilhelm & Grossman 2010). Laboratory methods are often considered the best way to establish the causal relationships among influences and outcomes. However, although the internal validity of experimental methods is often quite high, there are relatively few demonstrations of the ecological validity or real-world relevance of the findings. For example, the Decade of the Brain witnessed an explosion of research aimed at establishing the neural correlates of a range of psychological features, especially emotional and cognitive processes. In a typical study, standardized stimuli that are believed to evoke these processes are presented to a participant while neural responses are measured using imaging techniques.

The important question is whether these laboratory results translate into real-world emotional, cognitive, or behavioral experiences. To date, only a handful of studies have taken this additional step of evaluating the ecological validity of laboratory imaging results. Forbes et al. (2009) examined the real-world experience of positive affect in depressed adolescents who earlier participated in a functional magnetic resonance imaging (fMRI) paradigm to identify neural mechanisms associated with reward processing. As expected, neural processing related to reward anticipation and reward outcome during these tasks differed between depressed adolescents and healthy controls. Of most interest was the finding that activation in the caudate region, which distinguished the two groups, was significantly correlated with prompted participant momentary self-report of positive affect on mobile phones while in their natural environment. Specifically, within the depressed group, reduced caudate activation significantly predicted lower mean positive affect scores in the natural environment. Also focusing on depression, Walther et al. (2012) examined the ecological validity of results from diffusion tension imaging, which suggested less psychomotor activation. White matter integrity in two clusters associated with the motor

system was linearly associated with activity levels during waking hours as assessed using an actigraph worn on participants' wrists in both groups. In a similarly designed study, Walther et al. (2011) found that white matter integrity in the right supplemental motor area was negatively associated with real-world activity level in patients with schizophrenia but not in controls.

Several nonclinical studies warrant mention as well. Barrett et al. (2007) assessed amygdala activity in response to fearful faces using fMRI in undergraduates who had previously participated in an AA study of affective experience in daily life. Participants were prompted 10 times per day over 28 days to report on affective experience. fMRI imaging one year later revealed that those who had previously reported higher levels of negative affect showed greater amygdala activity in response to fearful face stimuli. Eisenberger et al. (2007) reported that neural activity elicited from a social rejection task was positively correlated to momentary reports of social distress over a 10-day period in a sample of young adults. Interestingly, although activity in three brain regions during an experimental prime for social rejection was positively related to average momentary social distress scores, activity in these brain regions during the task was not significantly related to the correspondence between momentary social distress reports and end-of-the-day reports of social disconnection. Thus, momentary reports had unique neural activity correlates, independent of what could be accounted for by end-of-the-day reports. Finally, Berkman et al. (2011) recently found that inhibition-related activation of certain brain regions in the laboratory moderated the association between momentary craving and subsequent smoking as assessed using mobile phones in a sample of adults participating in a smoking cessation program. Activation in the basal ganglia, in particular, predicted a reduction in smoking over the 21-day experience-sampling phase of the study.

Testing Gene × Environment Interactions

Models of gene × environment (G × E) interactions posit that specific "susceptibility genes" to psychological problems may be expressed under certain environmental conditions or in response to certain adversities. Since the publication of initial results from the influential Dunedin study (e.g., Caspi et al. 2003), hundreds of publications have examined the evidence for G × E effects in the manifestation of psychopathology. However, critics have pointed out the large number of failed replications as well as noted that very little variance in psychological problems or disorders is accounted for by these G × E effects (e.g., Duncan & Keller 2011).

Unfortunately, typical G × E studies measure environment influences in very imprecise ways. For example, adversity in childhood is often measured retrospectively, and even if the account is accurately recalled, the environmental influence is quite distal from the present symptoms or disorder manifestations that are being examined. Moffitt et al. (2005) recommend that measurement of environmental stress or adversity be prospective, cumulative, and proximal in order to adequately characterize environmental risk for psychopathology in G × E studies. Furthermore, Finan et al. (2012) note that AA methods can be used to improve both the reliability and validity of phenotype being investigated, and AA methods can help to identify and assess intermediate phenotypes (e.g., stress reactivity)

that are more relevant to the processes of the expression of the genes under certain environmental conditions.

To date, only a small (but growing) number of studies have used AA within the G × E framework to investigate psychopathology (for a recent review, see Finan et al. 2012). We present a few illustrative examples here. Gunthert et al. (2007) demonstrated that the mixed findings for the relationship between the serotonin transporter gene polymorphism (5-HTTLPR) and anxiety in previous studies appeared to be due to the insufficient measurement of the intermediate phenotype of anxiety/stress reactivity. In other words, findings for this association were contingent on the occurrence of stress-activated anxiety in daily life. Gunthert et al. (2007) note traditional studies that assess anxiety under mixed or no-stress conditions are unlikely to uncover this relationship because these studies do not consider the important environmental circumstances that foster this effect (i.e., stress in daily life).

Oorschot et al. (2009) summarized results from two clinical studies that examined emotional and psychotic reactivity to stress among patients with psychosis. These studies focused on the COMT Val^{158}Met and BDNF Val^{66}Met genotypes, and the authors found G × E effects for stress and increased psychotic experiences, stress and increased negative affect, and cannabis use and hallucinations (Henquet et al. 2009, Van Winkel et al. 2008). More recently, Ray et al. (2010) examined the effects of alcohol consumption on levels of self-reported vigor and of negative mood in heavy drinkers based on whether each individual was a carrier of a polymorphism on theORPM1 gene (associated with reinforcing effects of alcohol) and on the DRD4 gene (associated with drug reward). Drinkers with the targeted polymorphism on the ORPM1 gene reported higher levels of vigor and lower levels of negative affect as a function of increasing blood alcohol concentration in daily life. Carriers of the targeted DRD4 polymorphism reported greater urges to drink following increased levels of blood alcohol concentration.

Although the findings from these studies are interesting and illustrate another approach to measuring environmental influences on the expression of psychopathology, it is important to recognize some major limitations in these studies (see Dick 2011 for an overview of issues). First and foremost, the sample sizes in existing studies are much too small to reliably detect G × E effects, which themselves are notoriously small. Thousands of participants are needed. Second, factors that are considered environmental (e.g., stress, stress reactivity) may actually be under some degree of genetic influence, and it is necessary to test for the presence of gene-environment correlation as well. Finally, the inadequate scaling of environmental influences (i.e., how these are quantified) can lead one to conclude that a G × E effect exists when in fact it does not. In summary, we believe that AA studies are better suited to measure environmental influences in daily life (versus retrospective self-report). However, it will be necessary to collect AA data on much larger samples (and perhaps combine these) in order to adequately test G × E effects.

Challenges: Acceptability, Compliance, Privacy, and Ethical Issues

It is very easy to be “wowed” by the possibilities in AA given the advances in smartphone technology, the increasing portability and long battery life of sensors that can interact with

the smartphone, and the expanding possibilities of devices that can be used to both track and observe behavior. However, we must not be so enamored with the prospects of AA that we ignore or downplay important issues that should be considered and addressed before incorporating AA methods into clinical research or treatment. First, it is unlikely that AA methods will be readily adopted unless mental health professionals and clients or patients are comfortable with the technology. In addition, in the case of wireless technologies, patients (and clinicians) who live in areas not well served by wireless networks (e.g., rural areas of the United States) may experience some difficulty using handheld computers or smartphones. Second, some may also initially react to AA as potentially voyeuristic and intrusive (Conner & Lehman 2011). Therefore, it is necessary to anticipate these possible reactions and to be prepared to address these concerns with assurances regarding what specific data are being collected, what the data will be used for, how the data will be protected and not linked to individuals, as well as to discuss the limits of confidentiality (Conner & Lehman 2011, Goodwin 2011). Finally, AA methods are time intensive for patients and costly for clinicians and clinical researchers. Therefore, a demonstration of savings in time as well as incremental gain in knowledge is necessary before AA methods will be used routinely.

Even if participants and clinicians are open to using AA in clinical research or treatment, compliance with an AA protocol is a function of many additional variables including user-friendliness, burden of the protocol, and length of study period, to name a few. Fortunately, studies routinely document that individuals appear to be open to the use of wireless devices and are able to comply with prompts for assessments while in their natural environment (Ebner-Priemer & Sawitzki 2007, Hufford 2007, Shiffman 2009, Wenze & Miller 2010). However, one must not assume that high rates of compliance are guaranteed, and it is important to design studies and treatment trials that address reasons known to lead to poor compliance and to build in features known to increase compliance (Hufford 2007, Palmier-Claus et al. 2011). In addition, it is important to recognize that we know much less about compliance with interventions in the natural environment. For example, in the case of an interactive assessment with individually tailored moment-specific feedback, an individual must not only reliably report on his or her experience multiple times a day, but must also apply specific skills at the requested times to alleviate symptoms. Alternative strategies (e.g., self-recording audio or video using a smartphone) may be necessary to document the ability and willingness to implement the interventions when prompted to do so.

Finally, there are several privacy and ethical considerations for using AA. As with all electronic devices and communications used to document health status, privacy is a concern. Some of these concerns can be allayed by using password-protected devices and protocols, using data encryption and secure servers to house data, and providing HIPAA (Health Insurance Portability and Accountability Act of 1996) training to all those who have access to patient data. Other issues are perhaps more complex, such as how best to disclose data collected passively (e.g., through body sensors) if health problems are implicated, how best to respond to crises or emergencies that occur in the field (e.g., suicidality), and how to protect data that may indicate illegal activity (e.g., underage drinking, use of illicit substances). Recently, Shepard et al. (2011) interviewed their participants to better understand privacy concerns. Surprisingly, participants were open to having investigators

monitor the content of emails or texts, if data were analyzed immediately on the phone, without saving the email content itself. Given enough processing power on the smartphone, real-time analysis might be a promising way to address privacy concerns.

As mentioned above, it is important to build in certain safeguards and options into the design of the study or clinical intervention. It is always important to do extensive pilot testing of the protocol (Conner & Lehman 2011). In this way, one can get a better sense of the right balance between collecting relevant data and the intrusiveness and burden of the protocol. Another step that we use in our studies is for the investigator and some staff to actually participate in the full protocol before going into the field. This exercise can often provide insights about participant experience of the AA protocol, ultimately improving compliance and investigators' troubleshooting ability down the line. In addition to fully informing the participants as to the methods of the study, the nature of the questions and the data being collected, and the steps being used to ensure privacy and confidentiality, it is of course important to allow anyone undergoing AA to discontinue participation at any point in the study or trial. Finally, like others (e.g., Mehl & Robbins 2011), we encourage participants to be very open about the devices they are carrying or wearing while around family, friends, or coworkers as well as about the focus of the study itself (i.e., the focus is on the participant). In our experience, this serves several purposes: (*a*) Participants more quickly habituate to carrying and wearing the devices, reducing reactivity; (*b*) individuals who interact with the participant also habituate to the devices and are less likely to feel as though they are being spied on or are being included in a study without their consent; (*c*) if a family member or close friend objects, this becomes clear early in the study before too much time and energy is invested; and (*d*) it is more likely that the participant will actually carry and wear AA devices in his or her daily life.

Glossary

AA	ambulatory assessment
PDA	personal digital assistant
BPD	borderline personality disorder
EAR	Electronically Activated Recorder
GPS	global positioning system
MDD	major depressive disorder
NA	negative affect
PA	positive affect
HC	healthy control
SMS	short message service

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