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ELSEVIER

Review

Early warning signals and critical transitions in psychopathology: challenges and recommendations

Marieke A. Helmich^a, Merlijn Olthof^b, Albertine J. Oldehinkel^a, Marieke Wichers^a, Laura F. Bringmann^{a,c} and Arnout C. Smit^a**Abstract**

Empirical evidence is mounting that monitoring momentary experiences for the presence of early warning signals (EWS) may allow for personalized predictions of meaningful symptom shifts in psychopathology. Studies aiming to detect EWS require intensive longitudinal measurement designs that center on individuals undergoing change. We recommend that researchers (1) define criteria for relevant symptom shifts *a priori* to allow specific hypothesis testing, (2) balance the observation period length and high-frequency measurements with participant burden by testing ambitious designs with pilot studies, and (3) choose variables that are meaningful to their patient group and facilitate replication by others. Thoroughly considered designs are necessary to assess the promise of EWS as a clinical tool to detect, prevent, or encourage impending symptom changes in psychopathology.

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Keywords

Psychopathology, Ecological momentary assessment, Symptom change, Early warning signals, Critical transitions.

Abbreviations

EWS, Early Warning Signals; EMA, Ecological Momentary Assessment.

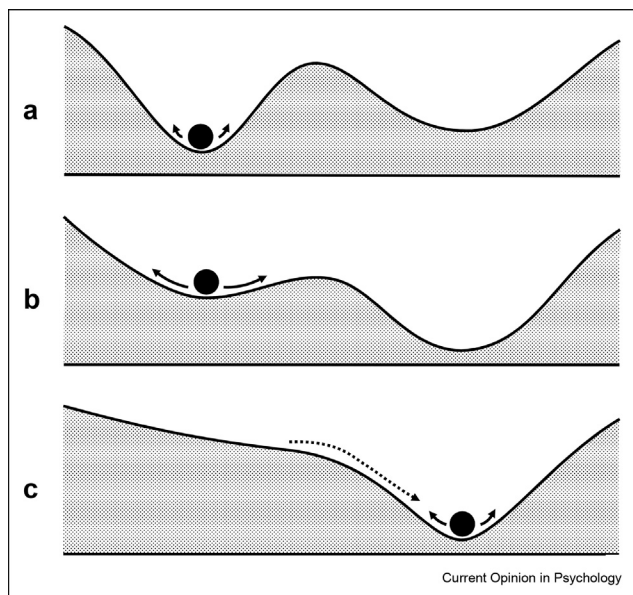
Introduction

In the search for a better understanding of the development and maintenance of mental illness, researchers have been drawing inspiration from the field of complex dynamical systems. Rooted in mathematics and physics, dynamical systems theory can be applied to the study of multidimensional processes of change, such as those occurring in ecology, finance, power grids, and, indeed, psychopathology [1–5]. Although discontinuous patterns of change (e.g., sudden gains and losses, symptom spikes, rapid early response, relapse) have been frequently reported in the field of clinical psychotherapy [6–10], traditional models of mental disorder typically do not provide an integrated conceptualization of the complex, varied patterns of symptom change that different individuals show. The dynamical systems framework has been suggested as a way to incorporate this wide variety of clinical change patterns into a coherent model that can further our understanding, early detection, and the treatment of mental illness [11,12*,13].

Within the dynamical systems conceptualization, an individual constitutes a multidimensional complex system of interacting components (e.g., behaviors, emotions, cognitions, and somatic experiences), which describe the system by their joint dynamic patterns over time [4,14*,15,16]. Individuals can move between different dynamically stable states (attractors), such as mental disorder or a psychologically healthy state. Psychopathology is theorized to occur when the system becomes more and more “attracted” to maladaptive functional patterns, which are maintained despite the negative effects on an individual’s well-being [17–19]. In other words, when moment-to-moment experiences and behaviors start to reinforce each other to create an overall more negative state, over time, the persistent presence of such negative experiences can become problematic to the point that they can be classified as the cluster of symptoms that can be recognized as a disorder [20].

One particular phenomenon has captured the interest of researchers for its potential clinical utility: early warning signals (EWS). In a dynamical system, a shift between states may appear abrupt and discontinuous

Figure 1



Visual representation of the system with alternative stable states, destabilizing, and restabilized.

The ball represents the current state of the system, and the basin in which it lies represents its current attractor. Other basins represent alternative attractors. For psychopathology, the ball symbolizes a momentary state (e.g., current emotion), and the attractors the possible states that the system can be in (e.g., equilibria of affect). In Figure 1A, the system occupies a stable (“deep”) attractor: if any perturbations push the ball away from the equilibrium position, it is unlikely to deviate much and will return quickly to the resting state. In Figure 1B, the system is destabilizing, and the temporal dynamics start exhibiting signs of “critical slowing down” and “critical fluctuations”: because the attractor has weakened, even small perturbations can cause the ball to move farther away and return more slowly. This shows as rising EWS, such as lag-1 autocorrelation and variance, and indicates that the system may be more likely to tip over into the alternative attractor. In Figure 1C, the system reaches a “tipping point” and restabilizes into the new attractor. The old attractor disappears.

on a global system level while it is preceded by a gradual destabilization, leading to EWS in the temporal dynamics of intensive repeated measurements of one or multiple variables at underlying (time) scales [21**]. For instance, as the system destabilizes before a transition, rises in the autocorrelation and variance of emotions may serve as EWS [22–24] (for more details, see Figure 1 and Table 1). For psychopathology, it is hypothesized that EWS can be observed in the dynamics of ecological momentary assessments¹ (EMA) of emotions, cognitions, and behavior, and may be detected *before* the system’s “tipping point” is reached and a critical transition occurs at the symptom-level [24,25**,26**]. Consistent evidence of EWS would provide an important empirical basis for adopting the

¹ Similar hypotheses have been investigated in clinical psychology using coded recordings of therapy sessions and dyadic interactions [29,30]. Researchers are also exploring whether EWS can be detected in passively collected physical measurements, like activity and heart rate data [56**,62].

dynamical systems conceptualization of psychopathology and the notion of critical transitions into the theoretical understanding of the development, persistence, and recurrence of mental disorders. Such evidence would also be of great clinical importance, as it promises the possibility to improve early detection of episodes of mental illness [27–29], to anticipate and prevent negative events such as depressive relapse and suicide attempts [26**,30,31], and, conversely, encourage positive symptom changes in the context of therapy [5,8,12*,13].

Yet, moving beyond dynamical systems as a narrative metaphor to explain clinical change phenomena involves both theoretical and practical challenges [32], and gathering the right data has been a major hurdle. In particular, it requires study designs that observe individuals *as they change over time* [23,33*], which implies methodological choices that differ from many previous EMA and intensive longitudinal designs where stationarity or “the absence of change” is assumed [34,35**]. Indirect evidence of EWS phenomena has been found at group level (e.g., Refs. [22,27,29,36–38]), but only a few studies thus far have measured how individual patients change over time and have been able to empirically test the hypothesis that rises in EWS occur before sudden symptom transitions [24,25**,26**]. The aim of this article is to outline a selection of challenges and considerations that should be heeded when designing studies on EWS in psychopathology (for a checklist overview, see Table 2 at the end of the article).

Challenge 1: defining transitions

The primary utility of EWS is that they precede upcoming critical transitions, which typically appear as large, sudden state shifts in the global behavior of the system [1]. What does a critical transition between stable states look like in the context of mental disorder? Because mental experience cannot be observed directly and has no absolute quantification, creating a one-size-fits-all definition of a critical transition in psychopathology is not straightforward. Careful consideration should be given to which constructs to measure (see Challenge 3), and to the fact that the idiosyncrasy of self- and clinician-rated symptoms means that potential critical transitions may have different magnitudes for different individuals, and different time spans in different disorders (see Challenge 2). Therefore, the first challenge is to define and identify relevant symptom changes that could constitute a critical transition in psychopathology.

The clearest transition is one between healthy and psychopathological states, which could be identified using existing, relatively well-defined diagnostic thresholds [12*]. However, for some individuals, the step across the diagnostic boundary may be small and

Table 1

A nonexhaustive list of early warning signals described by the underlying theoretical process and the statistical indicators.

Theoretical process	Description	Statistical indicators
Critical slowing down further detail, see [21**]	Close to a tipping point, the attractor loses resilience and becomes weaker, perturbations are more likely to push the system farther away from the center, and it takes longer for the system to return to the equilibrium.	Rises in autocorrelation (at lag-1) Rises in variance Rises in skewness Rises in connectivity (i.e., variable cross-correlations)
Critical fluctuations for a recent application, see [25**]	Once the existing attractor is fully destabilized, the system regains all its degrees of freedom, leading to fluctuations between all possible system states until it settles in a stable attractor.	Rises in dynamic complexity Rises in entropy Rises in variance
Flickering further detail, see [61]	If a system has two stable states and the dominant attractor is becoming weaker, perturbations can cause the system to "flicker" back and forth between alternative states, until one of the attractors becomes strong enough for the system to settle into one state.	Regime switching Bimodality Rises in variance Rises in skewness Rises in kurtosis

Note: definitions of important terms used in the table.

Attractor: a stable state of the system or dynamic regime; visible in the interactions and convergence of dynamic processes when observed over time.

Perturbations: external shocks or stressors.

Tipping point: the point from which the system undergoes a transition into an alternative stable state.

not meaningful; or conversely, symptom changes that remain above or beneath the threshold may still be relevant transitions between alternative stable states for an individual [39]. Therefore, apart from diagnostic shifts, researchers should search for transitions that are meaningful in the context of individuals' trajectories of symptoms over time [33*].

Quantitative methods can detect potential critical transitions as changes that stand out in the context of a particular within-person time series as shifts that are larger in magnitude than the natural variation expected in a stable or gradually changing system [18,28]. What is considered a large change in scores may be based, for instance, on thresholds established with a person's own baseline variance [40**], criteria for sudden change between therapy sessions [10,25**], a significant change in scores for a particular questionnaire [41], or statistically identified change points or regime switches [34,42,43]. Still, although quantitative approaches should work well on average [44], using only numerical data risks misidentifying some shifts that were experienced as (ir)relevant by the individual. Important changes may not be visible in the data if measurements are too far apart (see Challenge 2), or if the questionnaire lacks the relevant variable (see Challenge 3), and

conversely, sometimes numerically large changes are not judged as important by the patient themselves.

This leads to the other end of the spectrum: qualitative identification of critical transitions. Defining relevant symptom shifts by listening to the patient or clinician can improve the ecological validity of a study. However, retrospective reports can be biased, and the precise timings and impact of transitions can be hard to recall or put into words. In $n = 1$ case studies or in a clinical setting [45], transition identification can be strengthened by using various sources of information, both qualitative and quantitative. For larger group studies, using in-depth clinical interviews to identify transitions may be less desirable—although not unfeasible (see Ref. [46]).

To conclude, there is no standard way to identify potential critical transitions in psychopathology, and there is a need for exploratory and methodological studies to deepen the understanding of what critical transitions look like in psychological systems. Future studies may also include criteria for how long a symptom shift should be maintained to constitute a transition to a new state. Until there is more empirical evidence, researchers who want to conduct a confirmatory test of the EWS

hypothesis must thoroughly consider *a priori* how they will establish transparent, reproducible methods to identify transitions in their sample.

Challenge 2: timing all measurements appropriately

To capture a rise in EWS before a symptom transition in an individual, researchers must (1) select a population and period in which the transition has a realistic likelihood to occur, (2) estimate the change processes' duration, and (3) collect high-resolution data (i.e., many observations over time).

First, choosing a population in which symptom shifts are a common occurrence increases the chances of observing a critical transition and being able to test for preceding EWS. Clinical knowledge of a particular disorder and change process can help researchers to decide who to measure and when (for what to measure, see Challenge 3). For instance, discontinuous changes in symptoms are common in depression, even more so for patients receiving therapy [10,25**] or tapering antidepressant medication [46]. A practical advantage of studying a population with many transitions is that, in total, a smaller sample may suffice to find consistent evidence of EWS before transitions.

A second issue to consider is the observation period. Symptoms should be assessed often (in most cases, at least weekly), quantitatively and/or qualitatively, and long enough to observe the entire transition, within a time frame appropriate to the rate of change for the disorder: rapid-cycling bipolar patients may shift into manic and depressed states over the course of a few days (or even hours [47]), whereas reaching a state of remission from depression is considered a “rapid response” to therapy if it takes several weeks [9,48] and usually spans a period of months. Moreover, data collection should start while the system is believed to still be in a relatively stable state (Fig. 1A), gather enough data while the system is destabilizing (Fig. 1B), and continue at least until after the transition (Fig. 1C). Only with a comparatively stable period at the start of the time series can changes in system dynamics (i.e., EWS) be detected and used as indicators that the system is destabilizing and likely to “tip over” into an alternative state.

The third consideration is the determination of the (EMA) sampling regime. Different experiential processes fluctuate and change at different rates (compare a minute of irritation to feeling down all day), and therefore, the variable in which EWS will be calculated should be sampled frequently enough to capture those temporal fluctuations [14*,18,35**]. It is also worth considering that psychological time series are often noisy, and analysis methods typically require many (equidistant) data points to give robust results (e.g., [49–53]). Methods are being developed that may

elucidate optimal sampling frequencies in the future [54], but until we know the temporal resolution at which the fluctuations in momentary variables are best captured, high-frequency measurements (ideally multiple within the day and as many as possible) are the safest choice [55].

However, a tradeoff must be made between the need for high-resolution data and practical feasibility. For instance, although promising results have been obtained with once-daily self-ratings of depressed patients in treatment [25**], fast-changing systems, such as rapid-cycling bipolar cases, may require so many observations a day to get sufficient data between state shifts that it becomes practically or mentally unfeasible for participants. Although ambitious designs have been successful [8,46,56**,57], intensive longitudinal self-reporting can be burdensome and less feasible for some individuals or diagnostic groups [58]. Therefore, we strongly recommend running pilot studies to explore whether gathering sufficient high-resolution data is realistic and feasible for the intended population and change process.

Challenge 3: selecting relevant variables

Theory can guide the first steps in choosing variables in which to expect EWS. One of the properties of dynamical systems is that processes at different levels are interdependent: “zooming in” on symptoms of a disorder reveals the underlying moment-to-moment experiences (“I feel ...”, “I think ...”, “I am ...”) [20,59,60] in which EWS may be detectable². Indeed, momentary affect may be a logical micro-variable choice, as affective disturbances are involved in virtually all psychiatric disorders [15] and have been studied with EMA for years in many patient groups [58]. In addition, because variables are expected to become more and more alike (correlated) near the tipping point [21**,36], a few or as little as one variable could be sufficient to detect EWS and impending transitions. For example, changes in the dynamics of “I feel down” may precede a relapse in depression, as the item reflects a momentary experience of a core depressive symptom (i.e., prolonged feelings of sadness) [26**,32,40**]. Still, the number and content of the variables a researcher chooses to include may impact (1) the quality of their data: whether participant responses show variation and change over time in that variable; and (2) how broadly they can draw their conclusions: whether the variables show EWS for multiple people.

Including variables that can be expected to show natural variation at the chosen sampling rate (e.g., within the

² Even though, theoretically, EWS would also be expected to occur in symptom time series, symptoms are conventionally measured with retrospective questionnaires that cover periods of multiple days (e.g., the past week), which results in time series that lack the necessary detail to capture the dynamics of the system and the relevant rises in EWS.

Table 2

A conceptual checklist for designing studies on early warning signals and critical transitions in psychopathology.

Conceptual level	Questions to consider before starting data collection	See references in
Level of symptoms	In my study population ...	
	<input type="checkbox"/> What kind of discontinuous symptom changes are known from the clinical literature?	C1
	<input type="checkbox"/> How can a relevant transition be distinguished from normal variation?	C1
	<input type="checkbox"/> Could apparent symptom shifts be caused by external life events (e.g., a pet dying, or having the flu)? If so, can these be differentiated from true transitions by gathering contextual information?	C1
	<input type="checkbox"/> How fast can switches between states take place?	C1
	<input type="checkbox"/> How much time can a symptom change take to still be considered sudden, as would be expected of a 'critical transition'? And therefore, be relevant to predict with EWS.	C1
	<input type="checkbox"/> Over what time period can the system be expected to move from a relatively stable, into a period of destabilization, and finally, into a new stable state? Therefore, how long should the observation period be?	C2
Level of momentary experience	<input type="checkbox"/> How often do symptoms need to be assessed to ensure the full transition is observed and the timing of this transition can be accurately estimated?	C2
	In my study population ...	
	<input type="checkbox"/> At what sampling interval can the dynamics and EWS be accurately observed?	C2
	<input type="checkbox"/> How often do momentary affect variables need to be assessed to effectively a) capture the EWS dynamics and, b) have enough data and statistical power to find EWS before the transition is expected to occur?	C2
	<input type="checkbox"/> What momentary experience or emotion is theoretically most related to the symptoms and disorder?	C3
	<input type="checkbox"/> Are the chosen variables likely to show change as the system approaches a transition?	C3
	<input type="checkbox"/> Should the variables... <ul style="list-style-type: none"> • be relevant, reliable and valid for most individuals to allow generalizability, replicability and gather consistent evidence of EWS? • emphasize personalized signals, to predict impending symptom changes in the clinical context? 	C3
Overall design choices:	<input type="checkbox"/> Does data collection take place during a presumed change process (e.g., treatment, tapering of medication)?	C2
	<input type="checkbox"/> Can a pilot study be run to test the feasibility? That is, to find the balance between participant burden and compliance and the ideal overall duration and frequency of the measurements.	C2
	<input type="checkbox"/> Which analysis method can I use to detect EWS in my data?	C2
	<input type="checkbox"/> What is the goal of the study? For instance... <ul style="list-style-type: none"> – Exploratory work: methodological studies to improve understanding of what critical transitions in psychopathology look like. – Hypothesis testing: draw generalizable conclusions about the occurrence of EWS. – Clinical utility: find indicators and methods that could easily be implemented in clinical settings. 	C1, C3

Note: C, challenge; EWS, early warning signals.

day) and remain relevant over a longer period is important to ensure that the high-frequency observations actually measure the changing state of the system [32,35**]. Statistically, many EWS cannot be calculated when there is insufficient variance, and although creating aggregate variables from multiple items can make the analysis more robust to low variation and outliers, single items may offer better interpretability and replicability.

Choosing items that participants will find relevant is another important point. In the clinical context,

researchers (and clinicians) may personalize items and prioritize the best possible signal for an individual to monitor whether treatment is effective [8], or if the risk of relapse is rising [40**]. On the other hand, group studies (multiple within-person studies) may prefer to draw generalizable conclusions and choose a set of items that are expected to work well by showing variation and change over time for most people [33*].

To conclude, selecting variables in which one can theoretically expect and practically detect EWS deserves

further study in and of itself. Therefore, including as many EMA items as possible may be of limited value and would only needlessly increase the burden on participants. Researchers would do well to create designs with a selection of theory-driven variables and keep the future use in other studies or clinical practice in mind.

Conclusion

To make the most out of pioneering research on EWS in psychopathology, it is important to consider how to define transitions, time all measurements appropriately, and select theoretically relevant and practically useful variables. Furthermore, sound methodological choices cannot be based on theory alone, and in many cases, pilot data will be needed to construct a strong and empirical effective research design. Similar to a dynamical system, the methodological challenges involved in capturing EWS of upcoming symptom shifts are interdependent, and the success of a study depends on carefully weighing all the aforementioned design choices before data collection starts. Only then can we move beyond *post hoc* reasoning about EWS and test our hypotheses, and hope to bridge the gap between theory and clinical utility.

CRedit author statement

Marieke A. Helmich: Conceptualization, Writing – original draft; Merlijn Olthof: Conceptualization, Writing – review and editing; Albertine J. Oldehinkel: Supervision, Writing – review and editing; Marieke Wichers: Supervision, Conceptualization; Laura F. Bringmann: Supervision, Writing – review and editing; Arnout C. Smit: Conceptualization, Writing – review and editing.

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Conflict of interest statement

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* of special interest

** of outstanding interest

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