A Dynamical Systems View of Psychiatric Disorders - Theory

A Review

Scheffer, M.; Bockting, C.L.; Borsboom, D.; Cools, R.; Delecroix, C.; Hartmann, J.A.; Kendler, K.S.; van de Leemput, I.; van der Maas, H.L.J.; van Nes, E.; Mattson, M.; McGorry, P.D.; Nelson, B.

DOI
10.1001/jamapsychiatry.2024.0215

Publication date
2024

Document Version
Final published version

Published in
JAMA Psychiatry

JAMA Psychiatry | Review

A Dynamical Systems View of Psychiatric Disorders—Theory
A Review

Marten Scheffer, PhD; Claudi L. Bockting, PhD; Denny Borsboom, PhD; Roshan Cools, PhD; Clara Delecroix, MSc; Jessica A. Hartmann, PhD; Kenneth S. Kendler, MD; Ingrid van de Leemput, PhD; Han L. J. van der Maas, PhD; Egbert van Nes, PhD; Mark Mattson, PhD; Pat D. McGorry, PhD; Barnaby Nelson, PhD

IMPORTANCE Psychiatric disorders may come and go with symptoms changing over a lifetime. This suggests the need for a paradigm shift in diagnosis and treatment. Here we present a fresh look inspired by dynamical systems theory. This theory is used widely to explain tipping points, cycles, and chaos in complex systems ranging from the climate to ecosystems.

OBSERVATIONS In the dynamical systems view, we propose the healthy state has a basin of attraction representing its resilience, while disorders are alternative attractors in which the system can become trapped. Rather than an immutable trait, resilience in this approach is a dynamical property. Recent work has demonstrated the universality of generic dynamical indicators of resilience that are now employed globally to monitor the risks of collapse of complex systems, such as tropical rainforests and tipping elements of the climate system. Other dynamical systems tools are used in ecology and climate science to infer causality from time series. Moreover, experiences in ecological restoration confirm the theoretical prediction that under some conditions, short interventions may invoke long-term success when they flip the system into an alternative basin of attraction. All this implies practical applications for psychiatry, as are discussed in part 2 of this article.

CONCLUSIONS AND RELEVANCE Work in the field of dynamical systems points to novel ways of inferring causality and quantifying resilience from time series. Those approaches have now been tried and tested in a range of complex systems. The same tools may help monitoring and managing resilience of the healthy state as well as psychiatric disorders.

JAMA Psychiatry. 2024;81(6):618-623. doi:10.1001/jamapsychiatry.2024.0215
Published online April 3, 2024.

Multimedia
Related article page 624
Supplemental content
CME at jamacmelookup.com

Author Affiliations: Wageningen University, Wageningen, the Netherlands (Scheffer, Delecroix, van de Leemput, van Nes); Amsterdam UMC, Amsterdam, the Netherlands (Bockting); University of Amsterdam, Amsterdam, the Netherlands (Borsboom, van der Maas); Donders Institute, Nijmegen, the Netherlands (Cools); University of Melbourne, Melbourne, Victoria, Australia (Hartmann); Virginia Commonwealth University, Richmond (Kendler); Johns Hopkins University, Baltimore, Maryland (Mattson); Orygen, Parkville, Victoria, Australia (McGorry, Nelson).

Corresponding Author: Marten Scheffer, PhD, Wageningen University, PO Box 47, Wageningen 6700 AA, the Netherlands (marten.scheffer@wur.nl).

The current approach to diagnosing and treating psychiatric disorders is being questioned for several reasons, 2 of which stand out. First, symptoms people present with do not fit neatly into single diagnostic buckets. Thus, disorders exist on a spectrum of possible states (chronic anxiety, dysfunctional cognitions, depressed mood, etc) that are not clearly separated and vary widely between individuals.[1,2] Second, symptoms have a tendency to change over time. For a subset of patients, full recovery is never reached or they are confronted with relapse over subsequent episodes throughout life. After developing the first symptoms before adulthood, they may follow a roller coaster of disordered states over the course of their lifetime, reflected in a largely unpredictable succession of different diagnoses.[3-5] This provides a strong contrast with others who experience spontaneous recovery.[6-8] These features have prompted calls for a new paradigm to guide approaches that improve the well-being of patients.[4,9] Here, we show how dynamical systems theory may form the foundation of such a new paradigm.

A key point in our argument is that the risk of psychiatric disorders is related to dynamic resilience of the healthy mental state. An intuitive way of depicting the resilience of dynamical systems is by means of stability landscapes (**Figure 1**). We may think of resilience of the healthy state as its basin of attraction. As this basin shrinks, the risk increases that a stressful event pushes the system over its limits, causing a person to enter a self-propelling trajectory toward a disorder[10] (**Video**, A). It is widely recognized that persons differ in their intrinsic (trait) resilience.[11,12] In our dynamical systems perspective, resilience also changes over time. This, we argue, implies that monitoring and managing resilience of the healthy state of mind should be a central element in strategies for lifelong support of persons at risk of mental disorder.

How a Disorder Can Become a Trap

This way of depicting resilience of the healthy state corresponds roughly to the way psychiatry already looks at the concept, but there is a subtle twist. The term *resilience* has traditionally not been linked to mechanisms that cause persistence of a disordered state. Yet, perhaps counterintuitively, we may think of resilience of a disorder, capturing its tendency to persist in the face of efforts to reverse it. Such "bad resilience" may sound strange because the term *resilience* is reserved in psychology for the trait that may help a person recover. However, in systems theory, the term is used in a neutral sense. Applying this view, the healthy and disordered states are alternative attractors, both sustained by self-reinforcing feedbacks that can make them persist over time. The dynamics of systems with 2 alternative attractors are extensively studied across sciences, as they may explain shifts between contrasting states such as clear vs turbid lakes[13] or rainforest vs savanna.[14] To see how this works, consider for instance the latter ecosystems. Tree cover may vary widely, even if climatic conditions are the same. However, we usually find either closed forest or open savanna rather than something in between. The interpretation is that the intermediate state is unstable.[14] Either fire fueled by the grasses that grow between dispersed trees opens up the landscape, further leading to the typical savanna, or tree cover increases, which shades the grass and causes a moist microclimate where fires are rare, allowing the forest to persist and become denser.

Such self-reinforcing feedbacks are common not only in ecosystems, but also among the beliefs, emotions, and behaviors that shape our mental well-being. For instance, depressed mood may lead to a decline in social and physical activity, which in turn depresses the mood further. Associated beliefs, such as "I am worthless," may seem increasingly confirmed by selective information filtering, driving rumination, insomnia, and fatigue, which then further discourages social and physical activity, and so forth. It is easy to imagine how such feedbacks may cause a disorder to be a "trap" from which escape is difficult. On the other hand, the healthy state may also have self-reinforcing feedback mechanisms, in which a good mood invites social and physical activity, which reinforces the mood and a positive self-image.

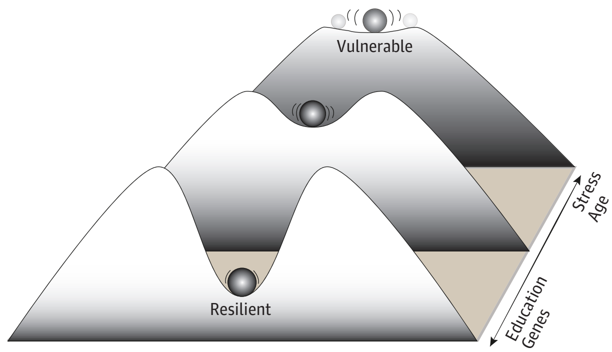
As in savanna vs forest, the intermediate state may thus be unstable, because those sets of feedbacks may propel an individual into either a depressed or a healthy state. Indeed, there is evidence that, just as in tree-cover data, the intermediate state can be relatively rare. For instance, individuals show a bimodal distribution of depressive symptoms over time, being mostly either depressed or healthy rather than something in between.[15,16]

Tipping Points and the Concept of Dynamic Resilience

While qualitative reasoning about feedbacks may help show how they can stabilize the healthy state as well as disorders, the key question is how dynamic resilience relates to that narrative. To stick to the example of depression, why can the healthy state become fragile enough to allow a minor perturbation (eg, a heated conversation) to cause a person to enter the vicious set of feedbacks, leading to full-blown depression? Or conversely: How can resilience of a depressed state decrease, making it fragile enough to allow recovery?

The generic theory of dynamical systems points to 2 fundamentally different kinds of forces here. First, there are the external conditions that matter. In a dryer climate, the rainforest becomes less resilient, and in a stressful environment, a person's healthy state may become less resilient. But second, and more challenging to understand, there is the effect of self-reinforcing feedbacks. When those are weak, the response of the system to changing conditions is smooth, but when self-reinforcing feedbacks are stronger, they may cause a more threshold-like response. If the self-reinforcing feedbacks are strong enough, they can cause the response curve to become 'folded' in the sense that for a given set of environmental conditions, there are alternative states possible (**Figure 2**A). How self-reinforcing feedbacks can have this effect may be shown mathematically or through a graphical approach (eAppendixes 1 and 2 in the Supplement). Here we focus on the consequences in terms of resilience, thinking of the feedback between behavior and mood.[17] Put simply, depressed mood leads to reduced activity, which in turn depresses the mood.

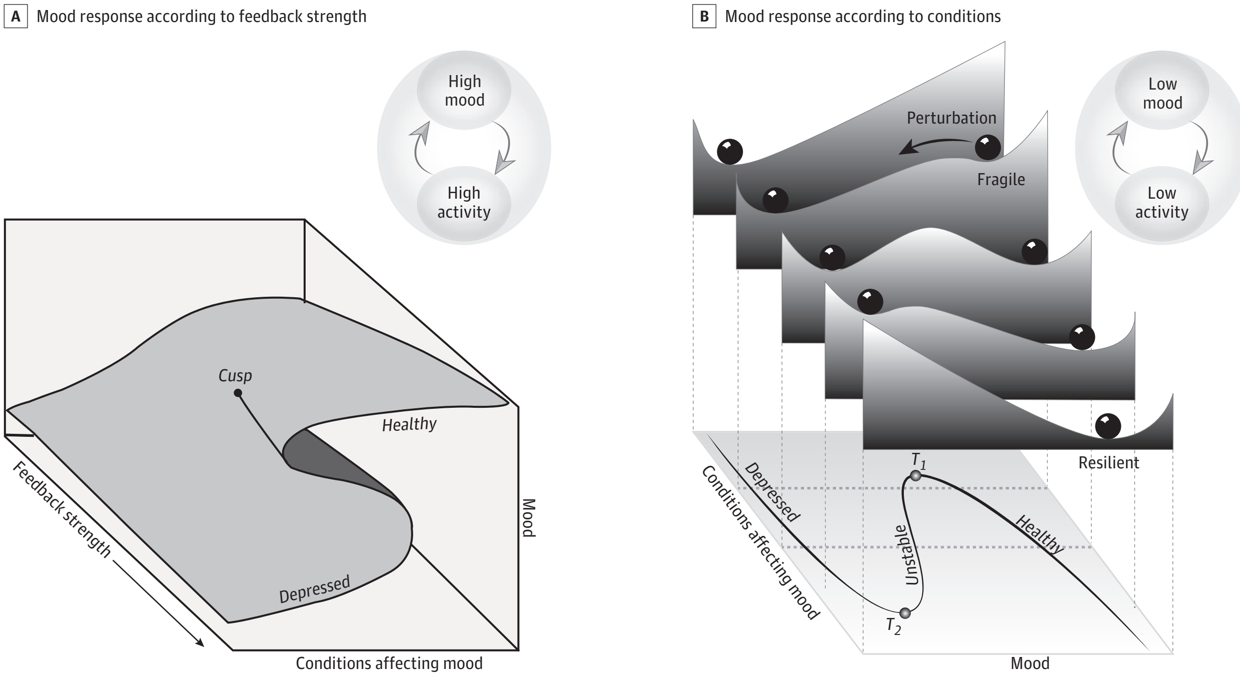
Figure 1. A Dynamical Systems Concept of Psychological Resilience Depicted as Basins of Attraction Around the Healthy State



For individuals in whom this feedback is weak (eg, because their activity pattern is relatively independent of their mood or vice versa), mood may vary smoothly with conditions such as the stressfulness of their environment (Figure 2A). By contrast, if the feedback is strong (ie, activity depends a lot on mood and vice versa), the healthy and the depressed state can be alternative stable states over a range of external conditions (Figure 2A and eAppendix 1 in the Supplement). In such situations, a shift from a healthy to a depressed state may come quite unexpectedly as a tipping point is reached. How this works can be intuitively seen from stability landscapes (Figure 2B). Here the valleys correspond to stable points (attractors) and the hilltops to unstable points (repellors) of the curve on the bottom plane representing the catastrophe fold for mood as a function of conditions. If a healthy individual (front stability landscape) is exposed to changing conditions (eg, an increasingly abusive interpersonal relationship) that affect their basal mood, we move to situations represented by stability landscapes in the background of the figure. Initially, the realized mood is only slightly reduced. However, the basin of attraction around this equilibrium shrinks. This implies a loss of resilience in the sense that only a small perturbation may eventually be enough to move the individual into the basin of attraction of the alternative depressed state (Video). If, subsequently, the conditions reverse (eg, the end of the abusive interpersonal relationship), the individual will have a tendency to stay in the depressed mood, because of the mood-activity feedback that makes the depressed mood represent an alternative stable state over a range of conditions. Another perturbation (a life event, exercise program, drug treatment, etc) can in principle induce a shift back to the healthy state.

The feedback between mood and behavior is just one example. Other disorders may be dominated by cognitive feedback loops that stabilize pathological beliefs. A well-known feedback mechanism in this context is confirmation bias. If we believe something, we tend to amplify evidence that confirms that belief, which in turn reinforces the belief.[18] Examples of effects of beliefs on perceived evidence are common among psychopathologies. For instance, in depression a belief like "I am a loser" may boost perceptions that others talk about you as a loser behind your back, consistent with that belief. Similarly, patients with anorexia nervosa who

Figure 2. How Resilience and Tipping Points Are Shaped by the Strength of Self-Reinforcing Feedbacks Such as the Interaction Between Mood and Activity



The surface in panel A shows how mood responds to conditions, given the feedback strength. When the feedback is weak, mood varies smoothly with conditions (the situation at the back of panel A). By contrast, where the feedback effect is strong, a person may be in a healthy state or trapped in a depression under the same external conditions (front of panel A). The consequences of latter situation are illustrated in panel B, showing how the healthy and the depressed state can be stable (valleys) whereas the intermediate state is unstable (a hilltop). As conditions change from the front to the back, the healthy state becomes less resilient, to the point that a minor perturbation can induce a shift into the depressed state. T_1 and T_2 are tipping points where either of the stable states disappear. To see how this model may be derived from a small set of assumptions, see eAppendix 1 in the Supplement.

believe they are fat misperceive their body as being fatter than is objectively demonstrable.[19] The feedback (belief → perceived evidence → belief) may make pathological beliefs a trap in the sense that they are difficult to escape from, even if reasonable arguments exist to abandon the belief.

The self-reinforcing feedbacks between beliefs and perceived evidence can be modeled in a similar way as the social and physical activity loops of the depression example, and the assumptions as well as the predictions of such a model are well in line with neurobiological evidence.[18] The belief component of disorders also implies a mechanism through which they may gradually become more entrenched. Each time they are activated, the pathological beliefs are more consolidated in neural circuits, making "unlearning" increasingly difficult. This fits with the idea that early identification of individual risk and prodromal symptoms is important for preventing the development of full-blown disorders as well as recurrences.[3] At such early stages, the beliefs are less entrenched, making them more receptive to contradictory evidence[18] and amenable to alternative interpretations,[20] strategies used in cognitive-behavior therapy and other psychotherapies.

Mental Health as a Complex Dynamical System

The feedbacks between mood and activity, or between belief and evidence, are of course part of much larger webs of factors that affect each other[2,21] (**Figure 3**). Such causal webs are widely studied using the dynamical systems framework. The elements of the web are then called variables, reflecting the fact that their value may change over time. Specific dynamical systems can be modeled by sets of differential equations that describe rates of change of each variable as a function of its current state and the state of other variables and drivers. For instance, to simulate the dynamics of a lake ecosystem, the populations of phytoplankton, zooplankton, fish, and other relevant variables could be encoded in a set of equations to simulate the response of this interactive system to changing temperature or pollution.[22] However, such an approach requires precise quantitative insight in the governing mechanisms.

In the case of psychiatric disorders, we are far from this situation. Many potential elements of the web of causal relationships that may shape a disorder have been described[23] (and patients are often aware of some links[24]). However, while qualitative mapping is possible, quantifying the forces in such causal webs remains beyond our reach. It may thus seem that we are left empty-handed when it comes to modeling the onset and evolution of psychiatric disorders in a quantitative way. Fortunately, however, we do not need a precise quantitative simulation model to obtain some key benefits of a dynamical systems view. If we assume that mental health is no exception when it comes to the generic laws that rule the dynamics of complex systems ranging from the climate to coral reefs, the continuous variability among patients, and the fact that the symptoms so often evolve and morph over time, makes sense. More importantly, new work on dynamical systems reveals how resilience and webs of causality may be inferred from times series. As will be discussed in part 2 of this article, such "equation-free" approaches may be used to analyze time series of mood, behavior, and other variables obtained from ecological momentary assessment techniques integrating wearable sensor data as well as self-reported mood and other information.

An Individualized View

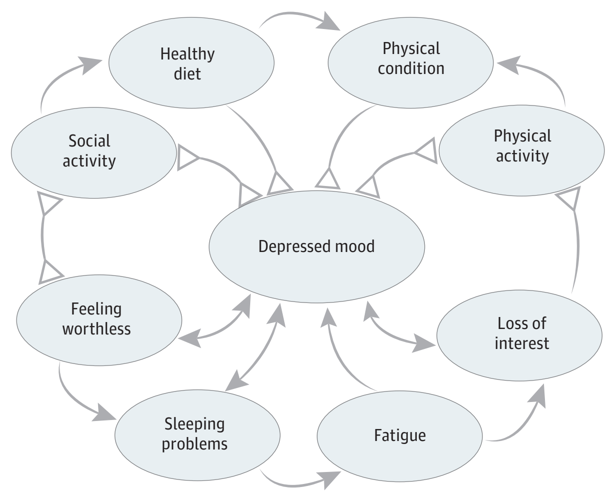
The network of multiple elements involved in disorders implies that the healthy state and its alternative disorder-attractors cannot be plotted as a simple 2-dimensional picture (Figure 1 and Figure 2). Instead, they are better seen as being embedded in a multidimensional space where each of the dimensions represents a relevant variable, such as valence of mood, amount of sleep, the extent of catastrophic thinking, etc (**Figure 4**). The position and resilience of attractors in this multidimensional space depend on an individual's history and genetic factors affecting the strength of the feedbacks that shape attractors. For instance, in some individuals a lack of physical or of social activity will have a stronger feedback effect on mood than in other persons,[25] and such intrinsic biological differences together with environment and life events are thought to determine how the same set of risk factors leads to different responses and disorders across persons.[26]

This view based on empirical observations is consistent with a dynamical systems framing where we should expect no two people to be exactly the same when it comes to the nature and resilience of the attractors in the stability landscape of possible disorders (Figure 4). In fact, for individuals who have a high trait resilience, the only resilient attractor may be the healthy state (Figure 4A). Disorders in such individuals have a resilience of nil, implying that they may appear as transient conditions but never as attractors in which a person can become trapped for prolonged periods. In view of the potentially endless individual differences, it may seem surprising that the basic structure of symptom correlations is still quite predictable. Thus, hills and valleys in the landscape may often be relatively similar across persons. This may be due to the fact that some of the causal relations shaping the web are in fact quite universal. Nonetheless, the large variation we see in patients fits the idea that individual differences in the strengths of feedbacks in the web of factors involved must lead to variation in the kind of states to which the system is attracted.

Understanding Change

Another implication of the dynamic web view is that the character and resilience of states will always change over time. Slow change may be driven, for instance, by the physiology of aging, but also beliefs may be slow to take hold or fade away. By contrast, thoughts and moods can fluctuate rapidly. Such rapid fluctuations can be triggered by external conditions but may be internally driven too. Intrinsic chaotic turmoil against a background of slow-changing resilience of alternative attractors is common in complex systems. Think of the unpredictable weather in a changing earth system with tipping elements ranging from the Amazon rain forest to the Greenland icecap.[27] The inevitable interplay of slow and fast variables in complex systems has several implications. As mentioned earlier, slow creeping change in resilience can affect the likelihood of flipping into another state (Video, A). As an example, aging reduces the resilience of humans and many of their subsystems regulating vital parameters such as postural balance, blood pressure, and cognition.

Figure 3. Hypothetical Web of Some Cognitive, Behavioral, and Affective Elements That May Aggravate and Stabilize a Major Depressive Episode



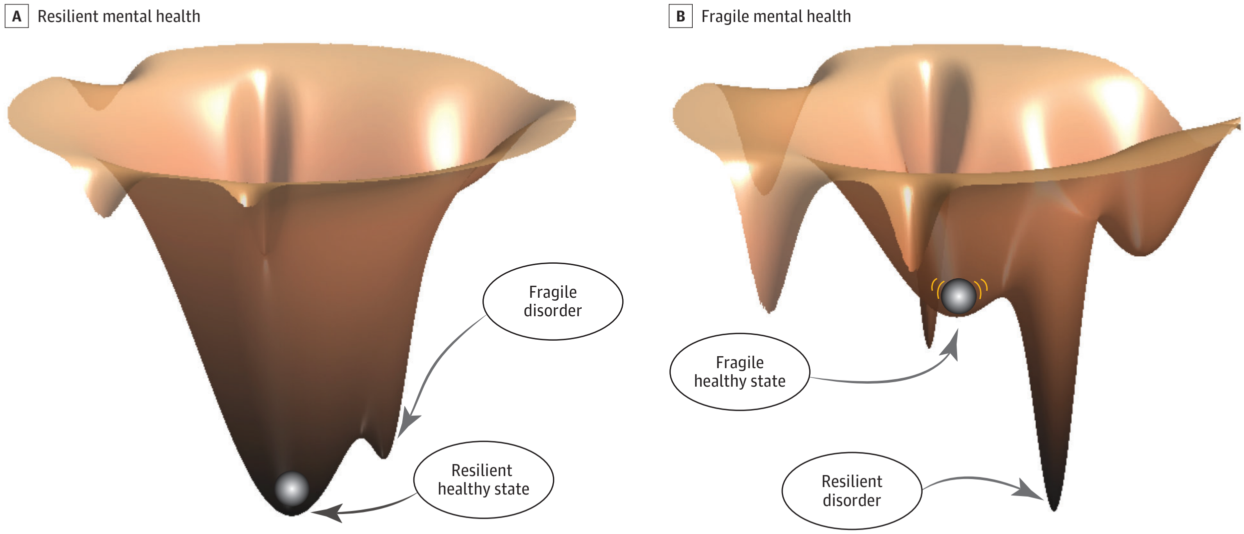
Positive effects are denoted by arrowheads, negative effects by triangles. Note that all feedback loops are reinforcing the depressed state. Consequently, resilience of the disorder may be reduced by addressing any of the behavioral or cognitive elements. The selection of elements and highlighted potentially causal relationships are just for illustration.

However, shifts between alternative attractors may also happen without underlying change in resilience (Video, B). In that case, in the long run, the average time a system stays in the alternative regimes depends on the size of their basins of attraction.[28] This might correspond to persons experiencing occurrence and remittance of major depressive episodes with various typical durations of the episodes and the periods in between.[8] The seemingly chaotic fluctuations that can drive the system to the alternative regime may often result from an inextricable mix of external influences and intrinsic amplifiers.[29] Imagine a thought/mood roller coaster bringing a person across a boundary where self-propelled change toward a full-blown depressive episode begins or even into a combination of arousal and sadness (mixed affective states) that could trigger a drive toward suicidal behavior. In short, we may think of dynamics over longer timescales as the result of an interplay of such fast fluctuations with the stability landscape shaped by slower mechanisms.

Lastly, an intricate type of dynamics can emerge when a slow variable responds to the fast ones in a way that causes cyclic flips back and forth between alternative attractors. In lakes, this can cause phases of clear and turbid water to alternate,[30] while in the Earth system it explains the wax and wane of ice ages,[31] and it could well be that in humans, transitions in bipolar disorder and other episodic diseases are driven by such mechanisms of autonomous destabilization of alternative states.[32]

This dynamic view of resilience is consistent with the observation that sometimes no intervention works while in other cases any

Figure 4. Mental Health Depicted as Stability Landscapes With Multiple Alternative Attractors Representing the Healthy State and Psychiatric Disorders



A, In a situation with resilient mental health, disorders have a low resilience, and episodes with symptoms will be brief if they occur at all. B, In vulnerable persons, the healthy mental state has a low resilience, and disorders are resilient alternative attractors in which the mental state can remain trapped for prolonged periods of time (ie, a resilient disordered state).

intervention can be successful. If the disordered state is much more resilient than the healthy state, even the best treatment will simply fail because the healthy state is too fragile and relapse will follow immediately. In the opposite case, when the disordered state has already become fragile, any intervention may work.

Outlook

The complexity of a multiplicity of morphing attractors mirroring lifelong roller coasters of disorders may seem a bit overwhelming. What might be practical clinical applications? Are there examples? Those questions are addressed in part 2, in this issue. There we will show that in addition to providing a framework for making sense of the elusive nature of disorders, the dynamical systems view we sketched opens up 2 practical perspectives. First, we may use a quantitative toolbox for estimating dynamic resilience from time series that reflect fluctuations in behavior and mood in daily life over time. This may help detect the optimal timing for interventions. Second, we may detect individualized intervention targets using dynamical systems techniques to detect the feedbacks that stabilize the healthy state or disorders in any given person.

ARTICLE INFORMATION

Accepted for Publication: January 11, 2024.

Published Online: April 3, 2024. doi:10.1001/jamapsychiatry.2024.0215

Conflict of Interest Disclosures: Dr Nelson reported grants from the National Institutes of Health, National Health and Medical Research Council, and Wellcome Trust and personal fees from the University of Southern California outside the submitted work. No other disclosures were reported.

Additional Contributions: We are grateful to Avshalom Caspi, PhD, Duke University; Laura Bringmann, PhD, University of Groningen, the Netherlands, and others for the liberal sharing of ideas during insightful discussions that helped over the years to sharpen the cross-disciplinary insights presented in this article.

REFERENCES

1. Borsboom D, Rhemtulla M, Cramer AOJ, van der Maas HLJ, Scheffer M, Dolan CV. Kinds versus continua: a review of psychometric approaches to uncover the structure of psychiatric constructs. *Psychol Med*. 2016;46(8):1567-1579. doi:10.1017/S0033291715001944

2. Cramer AO, Waldorp LJ, van der Maas HL, Borsboom D. Comorbidity: a network perspective. *Behav Brain Sci*. 2010;33(2-3):137-150. doi:10.1017/S0140525X09991567

3. Nelson B, McGorry PD, Wichers M, Wigman JTW, Hartmann JA. Moving from static to dynamic models of the onset of mental disorder: a review. *JAMA Psychiatry*. 2017;74(5):528-534. doi:10.1001/jamapsychiatry.2017.0001

4. McGorry PD. The next stage for diagnosis: validity through utility. *World Psychiatry*. 2013;12(3):213-215. doi:10.1002/wps.20080

5. Caspi A, Houts RM, Ambler A, et al. Longitudinal assessment of mental health disorders and comorbidities across 4 decades among participants in the Dunedin Birth Cohort Study. *JAMA Netw Open*. 2020;3(4):e203221-e203221. doi:10.1001/jamanetworkopen.2020.3221

6. Sobell LC, Ellingstad TP, Sobell MB. Natural recovery from alcohol and drug problems: methodological review of the research with suggestions for future directions. *Addiction*. 2000;95(5):749-764. doi:10.1046/j.1360-0443.2000.95574911.x

7. Whiteford HA, Harris MG, McKeon G, et al. Estimating remission from untreated major depression: a systematic review and meta-analysis. *Psychol Med*. 2013;43(8):1569-1585. doi:10.1017/S0033291712001717

8. Healy D. Melancholia: past and present. *Can J Psychiatry*. 2013;58(4):190-194. doi:10.1177/070674371305800403

9. Bhugra D, Tasman A, Pathare S, et al. The WPA-Lancet Psychiatry Commission on the future of psychiatry. *Lancet Psychiatry*. 2017;4(10):775-818. doi:10.1016/S2215-0366(17)30333-4

10. Scheffer M. *Critical Transitions in Nature and Society*. Princeton University Press; 2009:400. doi:10.1515/9781400833276

11. Friborg O, Barlaug D, Martinussen M, Rosenvinge JH, Hjemdal O. Resilience in relation to personality and intelligence. *Int J Methods Psychiatr Res*. 2005;14(1):29-42. doi:10.1002/mpr.15

12. Hu T, Zhang D, Wang J. A meta-analysis of the trait resilience and mental health. *Pers Individ Dif*. 2015;76:18-27. doi:10.1016/j.paid.2014.11.039

13. Scheffer M, van Nes EH. Shallow lakes theory revisited: various alternative regimes driven by climate, nutrients, depth and lake size. *Hydrobiologia*. 2007;584:455-466. doi:10.1007/s10750-007-0616-7

14. Hirota M, Holmgren M, Van Nes EH, Scheffer M. Global resilience of tropical forest and savanna to critical transitions. *Science*. 2011;334(6053):232-235. doi:10.1126/science.1210657

15. Hosenfeld B, Bos EH, Wardenaar KJ, et al. Major depressive disorder as a nonlinear dynamic system: bimodality in the frequency distribution of depressive symptoms over time. *BMC Psychiatry*. 2015;15(1):222. doi:10.1186/s12888-015-0596-5

16. Haslbeck J, Ryan O, Dablander F. Multimodality and skewness in emotion time series. *Emotion*. 2023;23(8):2117-2141. doi:10.1037/emo0001218

17. Lewinsohn PM. A behavioral approach to depression. In: Friedman RJ, Katz MM, eds. *The Psychology of Depression: Contemporary Theory and Research*. John Wiley & Sons; 1974:150-172.

18. Scheffer M, Borsboom D, Nieuwenhuis S, Westley F. Belief traps: tackling the inertia of harmful beliefs. *Proc Natl Acad Sci U S A*. 2022;119(32):e2203149119. doi:10.1073/pnas.2203149119

19. Challinor KL, Mond J, Stephen ID, et al. Body size and shape misperception and visual adaptation: an overview of an emerging research paradigm. *J Int Med Res*. 2017;45(6):2001-2008. doi:10.1177/0300060517726440

20. Brewin CR. Understanding cognitive behaviour therapy: a retrieval competition account. *Behav Res Ther*. 2006;44(6):765-784. doi:10.1016/j.brat.2006.02.005

21. Borsboom D. A network theory of mental disorders. *World Psychiatry*. 2017;16(1):5-13. doi:10.1002/wps.20375

22. Mooij WM, Trolle D, Jeppesen E, et al. Challenges and opportunities for integrating lake ecosystem modelling approaches. *Aquat Ecol*. 2010;44:633-667. doi:10.1007/s10452-010-9339-3

23. Wittenborn AK, Rahmandad H, Rick J, Hosseinichimeh N. Depression as a systemic syndrome: mapping the feedback loops of major depressive disorder. *Psychol Med*. 2016;46(3):551-562. doi:10.1017/S0033291715002044

24. Klintwall L, Bellander M, Cervin M. Perceived causal problem networks: reliability, central problems, and clinical utility for depression. *Assessment*. 2023;30(1):73-83. doi:10.1177/10731911211039281

25. Heller AS, Shi TC, Ezie CEC, et al. Association between real-world experiential diversity and positive affect relates to hippocampal-striatal functional connectivity. *Nat Neurosci*. 2020;23(7):800-804. doi:10.1038/s41593-020-0636-4

26. Nolen-Hoeksema S, Watkins ER. A heuristic for developing transdiagnostic models of psychopathology: explaining multifinality and divergent trajectories. *Perspect Psychol Sci*. 2011;6(6):589-609. doi:10.1177/1745691611419672

27. Lenton TM, Held H, Kriegler E, et al. Tipping elements in the Earth's climate system. *Proc Natl Acad Sci U S A*. 2008;105(6):1786-1793. doi:10.1073/pnas.0705414105

28. Arani BMS, Carpenter SR, Lahti L, van Nes EH, Scheffer M. Exit time as a measure of ecological resilience. *Science*. 2021;372(6547):eaay4895. doi:10.1126/science.aay4895

29. Bjørnstad ON, Grenfell BT. Noisy clockwork: time series analysis of population fluctuations in animals. *Science*. 2001;293(5530):638-643. doi:10.1126/science.1062226

30. Scheffer M. Population and community biology. In: *Ecology of Shallow Lakes*. 1st ed. Chapman and Hall; 1998:357.

31. Crucifix M. Oscillators and relaxation phenomena in Pleistocene climate theory. *Philos Trans A Math Phys Eng Sci*. 2012;370(1962):1140-1165. doi:10.1098/rsta.2011.0315

32. Bayani A, Hadaeghi F, Jafari S, Murray G. Critical slowing down as an early warning of transitions in episodes of bipolar disorder: a simulation study based on a computational model of circadian activity rhythms. *Chronobiol Int*. 2017;34(2):235-245. doi:10.1080/07420528.2016.1272608