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Review

Computational non-linear dynamical psychiatry: A new methodological paradigm for diagnosis and course of illness

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ABSTRACT

The goal of this article is to highlight the significant potential benefits of applying computational mathematical models to the field of psychiatry, specifically in relation to diagnostic conceptualization. The purpose of these models is to augment the current diagnostic categories that utilize a “snapshot” approach to describing mental states. We hope to convey to researchers and clinicians that non-linear dynamics can provide an additional useful longitudinal framework to understand mental illness. Psychiatric phenomena are complex processes that evolve in time, similar to many other processes in nature that have been successfully described and understood within deterministic chaos and non-linear dynamic computational models. Dynamical models describe mental processes and phenomena that change over time, more like a movie than a photograph, with multiple variables interacting over time. The use of these models may help us understand why and how current diagnostic categories are insufficient. They may also provide a new, more descriptive and ultimately more predictive approach leading to better understanding of the interrelationship between psychological, neurobiological, and genetic underpinnings of mental illness.

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1. Introduction

Many psychiatric disorders and symptoms wax and wane over time, with some exacerbations clearly associated with psychosocial stress and others that seem less linked to any precipitant and instead appear to occur randomly. Consider panic attacks, compulsive behaviors, obsessive thoughts, episodes of mania, and bouts of recurrent depression. When dissociated from stress, the pattern of waxing and waning of these disorders can appear independent of any underlying principles or explanation beyond spontaneous recurrences and remissions. Also, symptoms of seemingly different illnesses sometimes emerge or morph over time in the same person. More sophisticated and subtle computational analyses of the course of these disorders and their symptom composition may yield a better understanding of their temporal dynamics and eventually their phenomenology. Here “dynamics” refers not to psychoanalytical psychodynamics of intrapsychic life, but instead, to the larger computational study of complex systems that change over time.

Biological systems that oscillate, propagate waves, or communicate electrochemically with excitable tissue over time can appear to change with an irregular, random, or a periodic pattern. Yet, using non-linear dynamic analyses, patterns emerge that reveal an underlying organized complexity that is the mathematical basis of homeostasis.

‘Linearity’ essentially means that the effects in a system are proportional to their causes, and linear systems can be easily analyzed mathematically (Pooley, 2010). In contrast a ‘non-linear’ system exhibits unforeseen behavior even though its evolution in some future state can be predicted. This prediction requires more complex mathematical modeling. Non-linear systems can have stable states, periodic behavior or chaotic behaviors, depending on the initial state and parameters determining their evolution over time (Elbert et al., 1994). Brain researchers currently attempt to describe the temporal evolution of biological systems in terms of non-linear dynamics (Cartling, 2002; Lewis, 2005; Liaw and Berger, 1996). For example, in fear behavior, non-linear or random scanning of the environment for danger may represent a strategy to achieve rapid and highly adaptive responses when a threat is located (Pooley, 2010; Elbert et al., 1994). Non-linearity could be involved in the response to ambiguous, new and unlearned situations (Elbert et al., 1994). The brain is therefore a highly dynamic and adaptive

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non-linear system in which homeostatic mechanisms are sometimes destabilized in order to allow the emergence of entirely new and adaptive patterns of behavior. These are ultimately important on an evolutionary level and facilitate self-preservation (Pooley, 2010).

It has been suggested that some psychiatric phenomena likely follow these temporal instability patterns generating complex emotional/cognitive and psychosocial interactions leading to complex phenomenological presentations (Huber et al., 2001; Milton and Black, 1995). Non-linearity in psychiatric illness can manifest itself on multiple levels, from neural substrate to symptoms and social behavior. Some psychiatric researchers have already attempted to use non-linear dynamics in capturing complex psychopathology. For example, psychotic symptoms, dynamics associated with schizophrenia have been analyzed over a long time series (Paulus and Braff, 2003; Tschacher and Kupper, 2002). In these studies a large proportion of psychoses showed a non-linear evolution of the symptom's course. Non-linear analysis has also been applied to the study of complexity of recorded sleep EEGs (Keshavan et al., 2004; Lee et al., 2001). Hormonal oscillations have been described in female psychiatric patients (Rasgon et al., 2003). In major depression, increased predictability of time patterns in sleep and in waking EEG has been reported (Nandrino et al., 1994; Roschke et al., 1995). Another interesting example of interaction of different brain modes is recurrent mood switches in manic-depressive patients (Gottschalk et al., 1995; Post et al., 1977). Several studies have also employed non-linear and temporal mathematical approaches to study mood disorders, panic disorder and other anxiety states (Milton and Black, 1995; Bahrami et al., 2005; Rao et al., 2006; Bob et al., 2006; Rao and Yeragani, 2001). Therefore, interest in applying non-linear dynamic models to mental health has been present for some time now. Moreover, several scientists have commented that the field of psychiatry would benefit from systematic development of these computational strategies (Huber et al., 2001, 2000; Milton and Black, 1995).

The non-linear dynamic analyses of disorders have the potential to describe complex periodicity of their course (i.e. the frequency of episodes), can explain phase transitions (i.e. the waxing and waning of patients who go from being asymptomatic to meeting full criteria and back), and overall complexity of feelings, thoughts and behaviors (i.e. the range and scope of behaviors and thoughts associated with disorders and episodes - these tend to be more restrictive and stereotypical with decreased levels of complexity as compared to normal states) (Milton and Black, 1995; Huber et al., 2004). On a physiological level, the same models could incorporate the rhythm of neuronal gene expression, regulation of synaptogenesis, dendritogenesis, and neurogenesis, neurotransmission, regulation of oscillating neurochemical circuits, relationships between different neuroanatomical substructures, and, in space, the architectural branching of dendrites and neuronal connections that all appear to follow non-linear dynamical mathematical rules. In this paper we would like to consider a non-linear dynamical approach to phenomenology of mental disorders using the examples of anxiety and mood disorders. The goal is not to replace the Diagnostic and Statistical Manual of Mental Disorder's (DSM) diagnostic categories but rather to evoke the interest of the research community in applying mathematical modeling to the detailed study of the course of dynamic processes in mental illness.

1.1. Application of non-linear dynamics to phenomenology

The current approach to the phenomenology of mental illness is largely categorical. Categorical approaches to mental phenomenon were initially introduced to increase diagnostic specificity, treatment selection, and improve the prediction of prognosis. Recent work on revising the (DSM)'s categorical classification system aims

at enhancing reliability and validity of mental phenomenon (Phillips et al., 2010; Wittchen et al., 2010; Craske et al., 2010; Andrews et al., 2010). These efforts have renewed debates on how to best view and classify the mental phenomenon in general and anxiety disorders in particular (Shear et al., 2007; Hollander et al., 2007; Brown and Barlow, 2005; Coutinho et al., 2010). Over the past few decades exhaustive effort has been made in making the DSM classification system more reflective of clinical phenomenon by utilizing expert panels, making it more scientifically valid by conducting field surveys and making it a tool for further scientific exploration of biological and genetic underpinnings of mental disorders (Leclubier, 2008).

Several editions following the original DSM-III classification, (which appeared revolutionary twenty years ago) still fail to answer several important questions: Why do some clinical presentations such as agoraphobia fit multiple or no categorical diagnoses? Why do some clinical observations appear to transcend diagnostic categories over time? For example, why do some individuals who initially present with panic attacks go on to develop obsessive-compulsive disorder (OCD), bipolar disorder or psychosis? Why are biological and psychological interventions so similar for some drastically different diagnostic categories? Why do the categories fail to predict the outcome of different types of the treatments? Why are modern biological and functional imaging techniques failing to support DSM diagnostic categories? Why, despite advances in genetic sciences, are we still unable to identify genetic markers even for the most reliably diagnosed categories such as panic disorder or OCD? What should scientists do with "subthreshold" disorders (i.e., the conditions that do not quite meet full criteria of DSM)? The issues of current classification of mental disorders have been recently eloquently discussed by Hyman (2010).

These are very real and pressing questions for everyone who is involved in researching or treating mental illnesses. To address these issues scientists have debated the practicality of applying a dimensional approach to diagnosis and treatment (Okasha, 2009). Dimensional diagnoses consist of identification of certain symptom or phenotype dimensions (i.e. depressive, anxious, obsessive etc.) that are present in varying degrees in patients and that may depend more on specific biological markers, neuronal circuits and genetic vulnerability than observable behavior, as DSM mainly relies on. This approach has been explored by several scientists and appears to be equivalent if not superior to a categorical approach, although seemingly plagued by similar methodological deficiencies (Coutinho et al., 2010; Andrews et al., 2008). A multidimensional approach, however eloquently descriptive of an individual patient, will remain essential unhelpful if it cannot be applied to prediction of such things as course of illness and treatment outcome.

2. Competition principle and dynamical disorders modeling

We propose that one of the problems of poor predictive and descriptive ability of existing categorical and dimensional approaches may be that they are based largely on static or *cross-sectional* views of symptoms and symptomatic dimensions. In this approach, symptoms are still most often assessed as a snapshot in the present moment using specific psychometric assessments. In some instances DSM does make reference to temporal sequences such as behaviors that follow emotional states – for example the diagnostic criteria for obsessive-compulsive disorder state that the compulsion is done in response to the obsession, and that in panic disorder the avoidance behavior follows the initial panic attacks (American Psychiatric Association, 2000). However these only provide very limited and incomplete "short video clips" of these syndromes. For example, at times individuals will engage in compulsions without antecedent obsessions, and which may

appear to actually drive the obsessional thoughts. Moreover, these traditional approaches do not address the issue of persistence of symptoms over time, their purpose, and the functional interaction amongst different symptoms. Any symptom at any given time could be either a primary manifestation of a biological or psychological assault on the brain (e.g., panic symptom) or a secondary defensive response that represents the attempt to deal with the assault (e.g., coping response). For example, an escape reaction in itself in a patient with panic attacks may be a normal response in any individual to an extreme external or internal assault, given the degree of distress and anguish produced by the event.

We propose that further explorations of mental illness may benefit from a more *dynamic* view of mental illness whereby mental illness is viewed as interaction of key processes associated with pathology *in time*. In our recent paper we introduced a mathematical model using principles of non-linear dynamics that described cognitive and emotional processes that interact within the common dynamical space-time (Rabinovich et al., 2010). According to this model cognition and emotion compete for resources (i.e. a working space formed by emotion and cognition variables or modes that are changing in time) in a process known as Winner-Less Competition or WLC (Aron, 2007; Rabinovich et al., 2008). At the core of WLC is continuous competition of neuronal centers or circuits for the same resources (i.e. oxygen, glucose etc.). Cognitive and emotional processes are widely recognized as key elements in influencing human decisions impacting responses to all kinds of stimuli. The equations described in our recent paper (Rabinovich et al., 2010) are similar to those used in ecology and non-equilibrium thermodynamics to describe the competition of different agents for resources, i.e. generalized Lotka–Volterra kinetic equations that demonstrate well the spectrum of qualitatively different activity patterns regardless of the composition of the agents' intrinsic dynamics and interaction among them.

Fig. 1 displays the functional organization of the dynamical model, including decision-making and coping behaviors to a noxious trigger. The elements of the systems are connected by multiple feedback loops. The processes are not sequential and can start from any step and oscillate and interact in time (i.e., coping behaviors could affect further perception of the event and alter emotional reaction to, and cognitive appraisal of, the event via memory encoding). The dynamically interactive processes of panic disorder could be viewed as shown in Fig. 1. While the division of the system is helpful one has to understand that these processes are frequently overlapping and likely have overlapping neurocircuitry.

These processes reflect a continuous dynamical interaction between system components over time that result in the clinical manifestation of panic disorder. To this end, it does not matter whether perceptual sensitivity, cognitive distortions, an exaggerated emotional response, or a propensity toward inadequate coping started the process. Over time the system's interactions lead to the same presentation – panic disorder. Once the patients present to a clinician or researcher these systems are in a continuously interactive mode. That makes it exceedingly difficult to identify the underlying pathology by, for example, functional neuroimaging because of the number of neuronal systems involved. The complexity of the processes also creates difficulty in finding genetic determinants.

Another clinical example that can be understood in the framework of WLC dynamics is the interaction between anxiety and attention. Consider an adult who experiences intermittent states of emotional arousal (anxiety), which may reach higher level as a result of external events (e.g. news of a terrorist attack) and concomitant distorted cognitive appraisals (worry). These emotional arousal states, when exceeding some threshold, may then pull mental resources away from cognitive performance, particularly attention (Rabinovich et al., 2010). As the individual becomes further worried about his or her poor cognitive performance, this may subsequently result in greater time spent in higher emotional arousal states. Depending on when this person presents to a mental health clinician, he or she might receive a DSM-IV diagnosis of Generalized Anxiety Disorder (GAD) or, if such recurrent states trace back to childhood, Attention-Deficit Hyperactivity Disorder (ADHD), particularly if only the attentional symptoms are taken into account. Such narrow assessments can occur if the longitudinal and dynamic interplay of emotion and cognition are not taken into account. This example illustrates how WLC non-linear dynamics may better capture the phenomenology than linear and static diagnostic strategies.

The key feature in a computational dynamic theory of mental disorders is that within the “mental” space of humans, i.e. the space of interaction between perceptions, emotions, thoughts and behaviors (as in Fig. 1), we can conceptualize temporary structures that provide stability to the above cognitive and emotional processes. These structures interact within a sub-space that can be conceptualized as a channel that helps maintain a stable informational flow from one transient station (called a metastable state) to the next one, finally resulting in a behavioral outcome (see Fig. 2). Mathematically such channels are organized as “objects” that

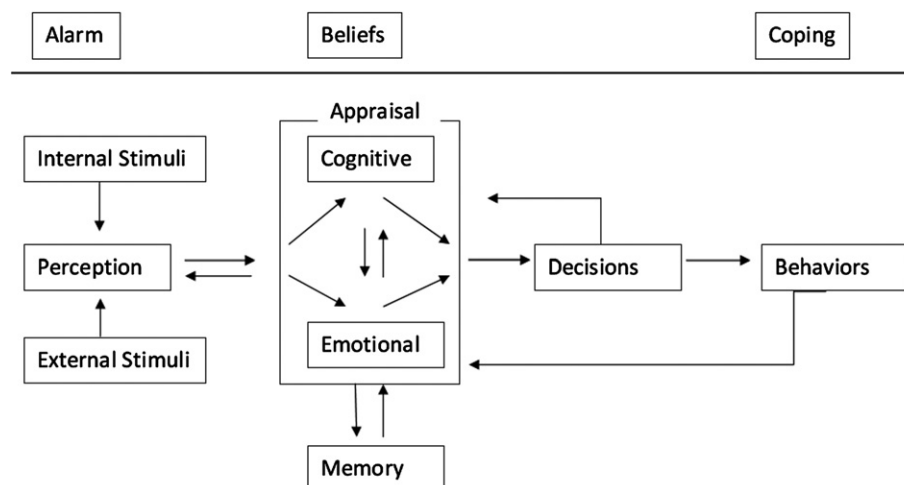


Fig. 1. Architecture of dynamical interactions within the model of anxiety disorders.

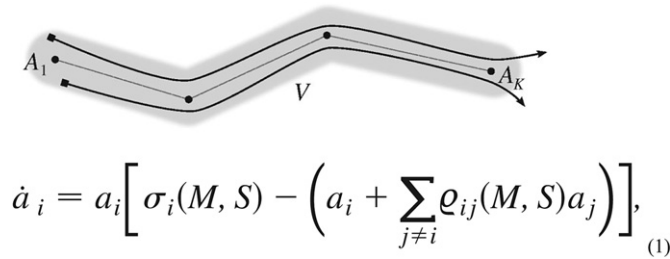


Fig. 2. Mathematical image of the stable heteroclinic channel describing behavioral steps within mental space-time. (Components of vector A – different metastable states, and V is a SHC, comp. with right panel in Fig. 2).

attract trajectory from neighborhoods in the transverse orientation within the channel. If the phase flow is compressed stronger in the transverse direction compared to stretching along chain, all trajectories in the vicinity of the heteroclinic sequence will become prisoners of this area – they cannot go away because of a strong compression. Such attractive area in the phase space along heteroclinic sequence is named a Stable Heteroclinic Channel (SHC). This mathematical object, as applied to understanding mental states, describes the working mental space that represents continuously generated and mutually modulated thoughts and emotions. Being a dynamic construct, the SHC has both spatial and temporal characteristics. The *spatial* or *topological* characteristic of SHC relates to 'areas' of *context* connecting metastable states i.e. steps. The *temporal* characteristic of SHC relates to the ability of the trajectories in the vicinity of metastable states to evolve, transform or generate new behavior over time.

The evolution of the system that has in a state-space a SHC could be described in a framework of a mathematical equation (Rabinovich et al., 2008). Here, a_i is the intensity of i -th competing mode, S is the input that captures all (important) external effects on the mental activity, M is the input from memory, σ_i 's are the increments that represent the resources available to the competitor i to prosper, and ρ_{ij} is the competition matrix that determines cognition/emotion transient dynamics. The set of variables $a_j(t)$ describes different brain modes of activity. It is important to understand that for the description of a typical disorder's behavior, it is enough to have only a few modes of activity i.e. perception, cognition and emotion. Because these modes are using the same resources (attention, memory etc., and energy) they compete with each other. The process of such competition is governed in the model by non-linear terms ρ_{ij} , $a_i(t)$, and $a_j(t)$. The parameters ρ_{ij} of such competition (non-linear interaction) depend on the environment and personal characteristics.

The equation reflects the relationship between several modes in the SHC that could be influenced by multiple *parameters* (i.e. memories, past experiences, physiological and hormonal states,

genetics, medications etc.). Complex mental activity could be represented by two (or more) channels in different sub-spaces that represent non-reproducible behavior: shrinking, expanding, splitting or merging with other channels.

In our WLC model cognitive-emotion dynamics are described by equations for the intensity of different mental modes. These modes compete with each other in time and each of them sequentially becomes a temporal winner. In the state-space of the model a temporal winner (metastable state) is represented by a saddle fixed point. Based on the landscape metaphor it is easy to see that two saddles can be connected by an unstable saddle separatrix (see the left panel in the (Fig. 3). This is the simplest heteroclinic sequence. In many-dimensional time-space (multiple interacting modes) heteroclinic sequences with many connected saddles could exist describing a complex mental phenomena (see right panel in Fig. 3; here we are indicating saddle fixed points that represent metastable states by components of vector S).

2.1. Obsessive-compulsive disorder

Certain dynamical features could signify potential channel instability representative of mental disorders such as obsessive-compulsive disorder (OCD) (see Fig. 4). In OCD unusual temporal features could, for example, represent an abrupt onset of pathological thinking leading to repetitive behavior that can emerge in the mental space. Let us consider, within the schematic presented in Fig. 4, the variety of behaviors typical of OCD.

The SHC (A) describes four steps (metastable states, represented by green balls) of the normal behavior of writing with a pencil (i.e. picking up the pencil, carrying it to the piece of paper, placing it on the paper etc.) leading to final completion of the activity denoted by the red ball. However, in the case of someone with OCD, at the fourth step the person may suddenly realize that the pen is contaminated and interrupt the behavior in order to wash his hands (SHC "R" – ritual – consisting of five additional steps such as picking up the soap, turning on the water, etc.). In the case of OCD at completion of R the behavior may not return to the original state A and instead could exit into several other possible SHCs representing different degrees of impairment dictated by emotion-cognitive appraisal of the situation. In case "B" the person could pick up the pencil and at the second step realize that the pencil is still dirty and go back to the ritual of washing (SHC R). In the example of SHC (C) the person may have touched the pen and immediately returned to ritual (R). SHC (D) represents a state in which the person with OCD, once his symptoms are triggered, stays in ritual without going back to the contaminated pencil until the resources are exhausted or some other factors come into a play.

This mathematical model permits us to precisely describe the evolution of the emotions, cognitions, and resulting behavior in mental space-time. One could see that similar models could be

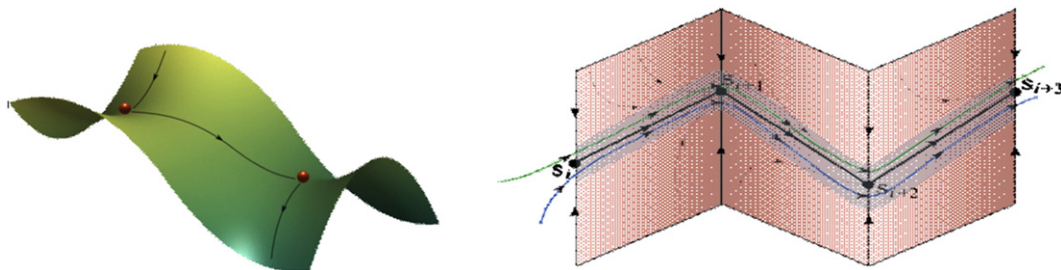


Fig. 3. Representation of a simple heteroclinic chain (left) and a robust WLC sequence of metastable states (right). In the phase space of a dynamical model a temporal winner is represented by a saddle fixed point. Based on this landscape metaphor it is easy to see that two saddles can be connected by an unstable saddle separatrix (see the left panel). This is the simplest heteroclinic sequence. In many-dimensional state space long WLC chains could exist (see right panel).

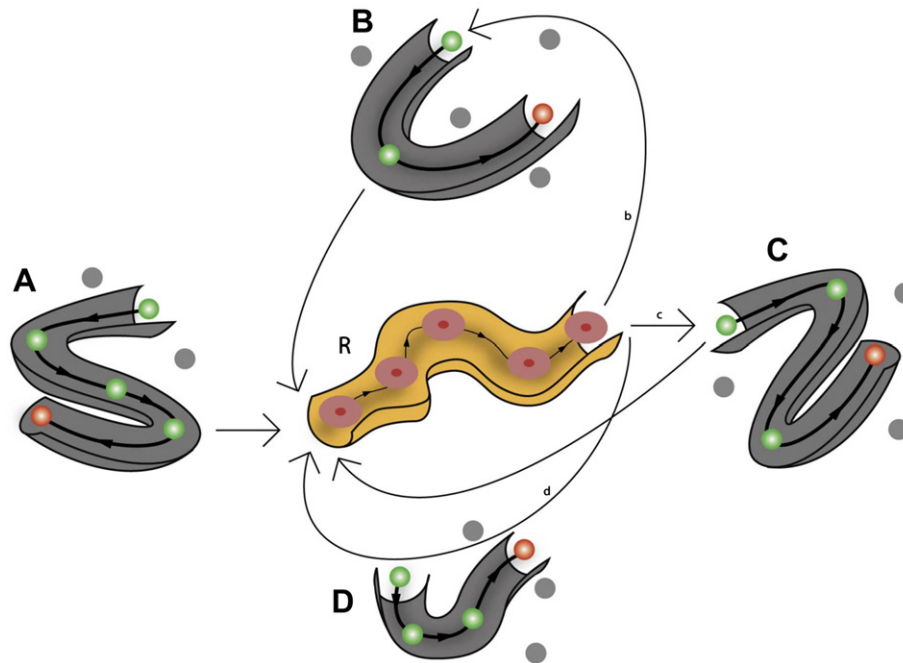


Fig. 4. Dynamical image of obsessive compulsive behavior. *Gray balls represent metastable states in mental space that did not become active.

easily constructed for other anxiety disorders such as panic disorder or social anxiety disorder. The time could be scaled down to hundreds of milliseconds to describe fast cognitive processes or up to years to explain the evolution of the symptoms over a longer time-course. By inputting new or changing old *parameters* influencing the model (i.e. sequential physiological, imaging, memory, personality measures, genetic characteristics, and environmental factors) we could become aware of the complex interactions between different modes within the common space-time.

The suggested model is very general because it is based on such fundamental principles as: (i) limited mental resources – energy, time, memory and attention capacity, (ii) existence of metastable states – states with characteristics that are not changing in finite time, and (iii) sensitivity of mental dynamics to environmental features – the sequential switching of metastable states depends on the perception of these external factors.

All of these principles separately are well known. However, to the best of our knowledge, this is the first attempt to combine them in a model that is able to describe the global brain mode dynamics. Thus, the structure of the model is universal and applicable for many different kinds of mental disorders.

The first principle of the model, for example, is well known in psychology as “mental ecology” or the “behavioral ecology principle” (Clark CWaD, 2003). This principle has also been extensively employed in neuroeconomics (Kenning and Plassmann, 2005), game theory (Lee, 2008), and decision-making theory (Doya, 2008).

Specific mental activities could transcend different DSM psychiatric disorders in the framework of this general model. This model also could clarify the emergence of different type of dynamics through different mental instabilities within the same diagnostic category. They can be analyzed by specific variants of a general model that can be formulated by specification of the control parameters. In other words, different mental activities map to different areas of control parameter space. These parameters are mainly types and numbers of metastable states, connection matrices that determine the modes’ interactions, and characteristic time scales (these are explicitly described in the new book on

mental dynamics (Rabinovich et al., 2012). The model is potentially universal in the sense that it proposes that different groups of patients are separated by a control parameter space. Because certain control parameters could be represented by specific therapeutic interventions or medications, the model could have diagnostic as well as clinical value.

2.2. The generality of the model

The model proposed by Rabinovich et al. (2010) is flexible enough to incorporate data from different parameter groups including psychometric, imaging and genetic domains. This can produce an individualized mathematical portrait of a given pathology that later could be clustered into overlapping groups for better identification of common pathological pathways. Admittedly, this may pose a challenge as to how to cluster these more complex descriptions. Nevertheless, this model could be implemented for diagnostic clarification that could perform better than a static DSM model and could help to clarify the relationship between phenotypical presentations and biological and genetic factors responsible for their development and maintenance.

This model could be implemented to improve our understanding and description of phenomenology. For example, observing interactions between processes in cognitive-emotional space may help understand similarity of the processes in different DSM anxiety disorders or it could clarify the differentiation of processes in disorders grouped into a “spectrum” on the basis of the main symptom similarities (e.g. Obsessive Compulsive Spectrum). Current diagnostic systems (either categorical or dimensional) represent snapshots of symptoms. However, dynamical systems describe *functional interactions* between different symptoms and domains of symptoms *in time*. In this way the model can be viewed more like a retrospective “movie”. That may be a reason why a good clinical interview is better than a structured interview for assessing and treating the patient. However, a clinical interview is frequently unstructured, and therapeutic success often depends on the interpersonal and

professional skills of the interviewer. Thus, combining a structured (cross-sectional) assessment with monitoring interactive processes or symptoms over time within a structured interview could be a first step towards optimizing assessment and treatment.

Structured interviews such as the SCID, CIDI or MINI (Williams et al., 1992; Wittchen et al., 1995; Sheehan et al., 1998) represent advances over previous unstructured assessments because they standardize the skills of the interviewer and control to some degree the patient–clinician interaction. However, these structured interviews still represent a static snapshot of the patient's psychopathology and as such could cause confusion. For example, a critical feature of panic disorder – panic attacks – can occur in multiple different situations, e.g., social situations (as in social phobia), situations reminding the person of a past trauma (as in post-traumatic stress disorder – PTSD), or when a person is confronted by a frightening event as in OCD or a simple phobia. Another example is a person who avoids freeways. This could be because of the fear of being trapped and having a panic attack (i.e., panic disorder with agoraphobia), or because a person has horrific images of his or her car getting into the crash (i.e., OCD with horrific imagery). Additionally, symptoms of agoraphobia could be present in major depressive disorder or generalized anxiety disorder (GAD) patients (who worry about nearly everything, including freeway driving) or as a simple phobia or as a consequence of a trauma (a car accident). Another interesting observation that the experienced clinician is familiar with is that some patients present with different disorders at different times of their life. An example is a patient who presents initially with panic attacks or social phobia and later perhaps with OCD or GAD, and then ultimately is found to have PTSD as the core psychopathology driving these presentations over time. To tease this apart it is important not just to know the symptoms of the disorders but also the interplay between different symptoms, what purpose they serve, and their development over time.

Similarly, there is a debate whether to remove OCD from the Anxiety Disorders category of the DSM. This is based on the fact that OCD sometimes occurs without anxiety (such as tick-like OCD, or contamination fear OCD that is based on disgust feelings rather than fear of acquiring an illness). Typically, OCD is fear-based with compulsions occurring in response to a fear trigger that is magnified by obsessional (often worst-case scenario) thinking. In some of these patients one cannot always trace the interplay between different symptom modes and instead patients may perceive their compulsions as arising “out-of-the-blue.” In some patients it simply means that they have less insight into their triggers of fears and obsessions and nearly automatically respond with compulsions. However, while many of these patients have similar presentations (i.e., compulsive behaviors) they may not represent the same disorder. These patients may have compulsive ticks, perseverations or ruminations that have different psychopathological underpinnings, etiologies and treatment responses. Lumping together all patients exhibiting compulsive behaviors into an “OCD spectrum” runs the risk of lumping together drastically different syndromes such as habits and neurological perseveration secondary to brain injury. Dynamic formulations of these disorders, when the data is assembled into mathematical models such as that proposed by Rabinovich et al. (2010) and American Psychiatric Association (2000), will represent significantly improved conceptualizations and will likely lead to better understanding of their psychopathology and clinical treatment responses.

In addition, this model could help clarify the relationship between phenotypical presentations and biological and genetic factors responsible for their development and maintenance. The present phenotypical confusion makes it difficult to identify and synthesize information about biological and genetic underpinnings of categorically-defined disorders. The proposed model addresses

this issue by looking at the biological underpinning of processes that create phenotypical presentations retrospectively (i.e., a “movie”) rather than relying on a diagnostic snapshot. The estimation of the parameter values corresponding to observed behavior, and reflecting the distance to the edge of instability (in the control parameters of space) is a way to predict the evolution and the outcome of different psychiatric disorders.

How do these space-time characteristics of behavior relate to traditional statistical views of mental disorders? Temporal information is important for estimating the probability of the emergence of disorder-specific behaviors over long time intervals. It is important that analyses of long time intervals in the vicinity of the edge of stability provide us with a connection to traditional statistical characteristics of behavior. In fact, the corresponding numbers are the averaged characteristics of time series analyses within finite intervals of time. Such interval can be as short as milliseconds and as long as weeks or even months.

2.3. Adaptability of the model to bipolar disorder

The above model applies not only to anxiety but also to other mental disorders.

In fact, dynamical assessment has previously been applied to mood variability in specific disorders such as bipolar disorder and depression. Periodic fluctuations of problematic thoughts and emotions among patients with bipolar disorder and personality disorders may produce non-linear dynamical patterns of daily mood variation (Warren and Hawkins, 2002). Several studies adapted dynamic modeling to study depression and bipolar disorder psychopathology and treatment (Gottschalk et al., 1995; Tretter et al., 2011a,b; Wehr and Goodwin, 1979). Mood dynamics are important in bipolar illness; random dynamics in controls were found to differ from the chaotic dynamics among bipolar outpatients and rapid cycling among bipolar inpatients (Goldberger et al., 1996). This pattern of randomness-to-periodicity in control-to-chaos supports the idea that changes in finite time, and sensitivity of mental dynamics to environmental features, could represent the sequential switching of metastable states that depends on the cognitive/emotional appraisal, as we show in our model.

To further understand the dynamical nature of bipolar disorder in a framework of the general model we have to specify the competitive mental modes. This can be done by employing several different modes that represent a specific cognitive activity, for example, decision-making, utilizing short-term memory, and attention. The next step is to specify three emotion modes that represent normal mood (mode N), depression (D) and euphoria (E). Normal subjects and bipolar patients will demonstrate different types of behavior i.e. different dynamics that are projected to different areas of parameter space that are separated by ‘bifurcation’ boundaries. The transition through such boundary translates to the emergence of new dynamics. Our computer modeling of the general model with six agents (Varona et al., 2002) demonstrated that typical regimes for such a system are: (i) two agents' activities are close to zero (modes D and E), one is close to constant (N), and the rest demonstrate some pulsations (cognitive modes); (ii) rhythmic switching between modes D and E with some cognitive activities in-between; and chaotic sequential switching between D and E with random time intervals between them. The last case corresponds to bipolar disorder presentation dynamics. The mathematical image of such dynamics is named as a strange attractor (see, for example (Rabinovich et al., 2012) and the corresponding time series looks like:

NDNNENDDNEENDNENNDNNE...

This exactly corresponds to data recently reported by Bonsall et al. (2011) that analyzed the dynamics of mood switching in bipolar disorders.

2.4. Future implementation of mathematical modeling

In order to implement this theory in practice the research community needs to take several steps. First, we need to develop retrospective clinical interviews to reliably capture the evolution of symptoms since their origin. We need to also be able to measure the severity of core symptom domains over time and the interplay between these domains within certain time frames. We have to take the developmental history of each symptom in a structured way while taking into account that some of them developed in response to the other. By doing so we will be able to better understand the interaction between the system of symptoms or modes in time. For example, perceptual and emotional–cognitive interactions leading to specific decisions and coping strategies need to be elucidated. The data on evolution of a single symptom or symptom clusters interacting with each other and systems unifying several symptom clusters over time could significantly improve our understanding of biopsychosocial processes underlying the disorder. However, psychometric instruments that are able to perform this task are not yet available.

In some ways this method will be similar to a clinical diagnostic history, which is still a “gold standard” in assessing symptoms and most useful in treating psychiatric patients. A reason why a clinical diagnostic history from an experienced clinician may be the best approach to date is that human cognition may operate in an intrinsically Bayesian framework of probabilistic thinking (Tenenbaum et al., 2006); that is, it is based on prior probabilities from specific knowledge and pattern recognition from general experience. The experienced clinician is flexible in his or her approach, creating an iterative process that continually updates probabilistic thinking about course of illness and treatment response based on new knowledge. Yet in current clinical practice the effectiveness of this may be limited if part of the decision-making process is built on trying to fit observations into inadequate, linear frameworks provided by static diagnostic categories. Operationalizing the application of both Bayesian and non-linear mathematical modeling could greatly assist in training less experienced clinicians and could be applied to scientific investigations. Initially this way of viewing the patients could be added to the current DSM specific techniques as a supplement in a way it has been done with the concept of dimensional diagnoses (Andrews et al., 2010).

Let us also consider the treatment of an episode of major depressive disorder. During an episode, thoughts become so rigid and stereotypical that cognitive-behavioral therapists identify and target characteristic dysfunctional modes of thinking. Patients lose their ability to think flexibly about themselves, their world, and their future. Cognitive-behavioral therapy (CBT) helps them to be less rigid by questioning their silent assumptions (beliefs) and practicing more complex responses by considering alternatives to their automatic thoughts and more flexible coping behaviors. By doing so, their emotional reactions to their interpretations are dampened and their behavioral repertoire becomes more flexible and complex. When successful, the CBT process increases depressed patients' complexity of reactions and allows them to become more resilient to stress.

Applying this method to the clinical model, we can also understand how an episode of an illness occurs with stress. Is it as simple as a linear, sequential relationship during which a stressor occurs followed by an accordingly severe episode? Or is it that a series of stressors or persistent stress finally reaches some threshold that causes a sudden change in one's state? Do the symptoms start all together or does one symptom start and the others follow in sequence? Can mini, subthreshold episodes start and then fail to reach threshold levels and then recede? If so, how

does this happen and what are the underlying physiological principles that determine these patterns?

3. Conclusion

Using non-linear dynamical modeling will greatly assist our understanding of mental phenomenon and help establish the relationship with neural systems and genetic factors, which could be easily integrated into the model. The use of such mathematical modeling may be complex and may not be well understood currently by the whole medical community. However, this should not deter scientists from testing it in future studies. Non-linear dynamics are not currently taught within the curriculum in psychology or medical schools. Yet the process of adapting it may be similar to that of higher levels of statistics, which was also not commonly taught or widely used by researchers as recently as just a few decades ago. Eventually this could lead to a better understanding of mental dynamics and biological underpinnings of the complex emotional-cognitive-behavioral phenomena that are currently classified as mental disorders.

Conflict of interest

No relevant conflicts of interest for any of the authors.

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