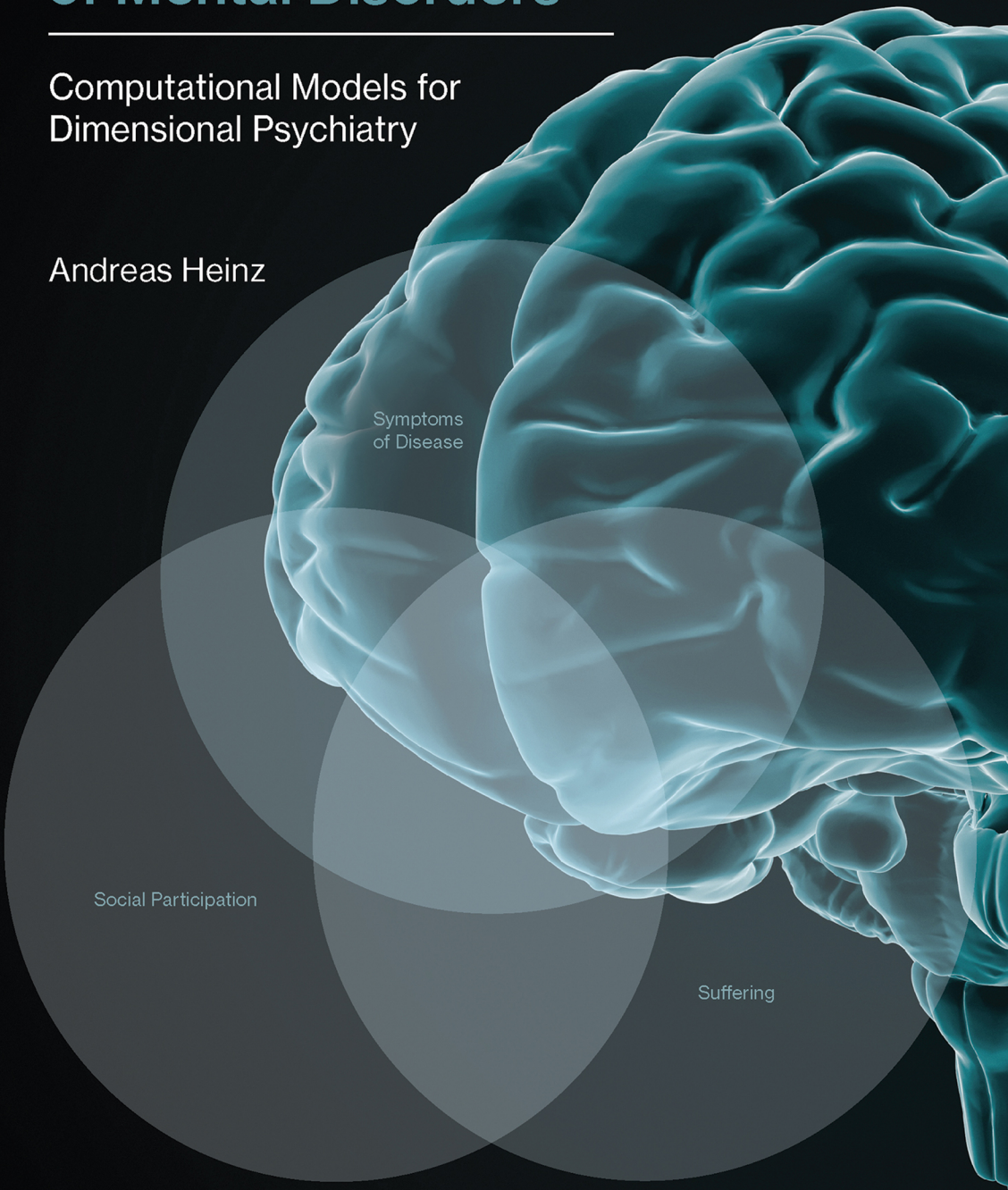
A New Understanding of Mental Disorders

Computational Models for Dimensional Psychiatry

Andreas Heinz



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Preface

The times they are a-changin'
—Bob Dylan

Research on the neurobiological correlates of mental disorders has seen a dramatic increase in both the scope and depth of investigation. Nevertheless, to date, many mental disorders are still classified according to criteria that solely rely on the manifestation of clinical symptoms and their change over time. To some degree, this situation is comparable to the state of knowledge with respect to "stroke" before cranial computed tomography was introduced into routine clinical diagnosis more than 40 years ago. With the help of such imaging methods, ischemic versus hemorrhagic strokes could easily be distinguished, and treatment was adjusted accordingly. Similar hopes were raised when functional magnetic resonance imaging (fMRI) started to be widely used in neurobiological research on mental disorders. Today, there is an abundance of findings relating certain cognitive experiences to their respective activation patterns. However, the impact of such imaging technics on clinical diagnosis and treatment with respect to most mental disorders was rather limited. Accordingly, two conclusions can and have been drawn.

The first one questions the validity of current diagnostic categories and suggests that neurobiological findings do not help to guide treatment decisions because these diagnostic categories rely on inadequate classifications of mental disorders. Accordingly, this dimensional approach suggests not to start with traditional diagnostic classifications (e.g., the distinction between schizophrenia and bipolar disorder) and then look for neurobiological correlates that clearly distinguish these two disease categories from each other. Instead, research should focus on the neurobiological correlates of key cognitive mechanisms (including working memory performance)

and assess their various degrees of alteration across established nosological boundaries.

A second, not mutually exclusive approach suggests that our current and most widely used imaging techniques are not sophisticated enough to capture the relevant neurobiological alterations in mental disorders. This computational approach suggests that beyond identifying activation patterns that are associated with certain mental operations, mental operations themselves should be analyzed more diligently. Specifically, computational models should be generated that reflect decision-making processes and reveal key computational steps guiding behavior, which can then be used to search for biological correlates of these computational operations. A famous case in point is computation of an error in reward prediction, which drives reinforcement-based learning and has been associated with the amount of phasic dopamine release in the ventral striatum and related brain areas.

This book focuses on both approaches and tries to link them with a new look at the classification of mental disorders. Our approach supports the idea that key mechanisms of learning and decision making including Pavlovian conditioning as well as model-based and model-free instrumental behavior should be computationally modeled and assessed in different mental disorders, thus following a dimensional approach instead of limiting research to one traditionally defined disease category at a time. Furthermore, we suggest that current clinical classifications have become too complex and tend to label common states of human suffering as disorders, thus failing to focus on severe diseases including dementia, addiction, as well as major affective and psychotic disorders. We suggest that traditional disease categories have their clinical value, yet nevertheless are in need of critical reflection including a foundation in a philosophical anthropology, which reflects and respects the diversity of human experiences and limits itself to describing key mechanisms required for individual survival and living in a shared world with other human beings. It is to patients who experience severe mental disorders and display impressive creativity when trying to cope with their challenges and their therapists that this book dedicated.

Acknowledgments

This work would not have been possible without my academic teachers, Prof. Dr. Horst Przuntek, who introduced me to neurology and accompanied my professional development for more than a decade; Prof. Dr. Hanfried Helmchen, whose focus on ethical issues in psychiatry is inspiring psychiatrists to this day; Dr. Daniel R. Weinberger and Dr. Markku Linnoila, who shared their profound experiences with me during a stay at the National Institutes of Health; Prof. Dr. Fritz Henn and Prof. Dr. Karl Mann, who accompanied my professional development during work at the University of Heidelberg; and Prof. Dr. Axel Honneth and Prof. Dr. Hans-Peter Krüger, my philosophical teachers. This work would not have been possible without grant support provided by the European Union, the Deutsche Forschungsgemeinschaft (DFG), and the German Ministry for Research (BMBF). I am deeply indebted to a large number of friends and coworkers whose main publications are quoted within the following pages. I would also like to thank my family for their continual support and last but not least give my special thanks to all the patients and probands who participated in our studies. Experiencing mental disorders can cause tremendous suffering but also provide an unusual and therefore very important perspective on human life. Patients with depression are known to be more realistic and rational than nondepressed subjects (who generally tend to overestimate their individual importance), subjects with psychosis experience the fragility of our common understanding of human interactions, and patients with addictions encounter human desire in its deepest degree. All these experiences are not only deeply human but also provide alternative and often very creative views on our lifeworld, and while this book focuses on mechanisms trying to explain mental disorders, the contribution of such individual experiences to a deeper understanding of human life cannot be underestimated.

1 Introduction

Psychiatric research is impressively successful: neurocircuits have been identified that are activated when humans are confronted with affectively positive or negative stimuli; it has been elucidated how these neurocircuits are modulated by neurotransmitters such as dopamine and serotonin; genetic and environmental effects have been described that modulate such neurotransmitter systems; and these insights have helped us to better understand the effects of medication, as well as some psychotherapeutic interventions (Meyer-Lindenberg, 2010; Heinz et al., 2011; Wang and Krystal, 2014). Moreover, basic research has helped to identify the exact computational roles that certain neurotransmitters such as dopamine play in modifying behavior, and the same mathematical tools can be used to formalize empirical accounts of individual variability, providing us for the first time in the history of psychiatric research with the possibility to use the same computational approaches to describe behavior and its underlying neurobiology (Corlett and Fletcher, 2014; Friston et al., 2014). Instead of trying to correlate mood states as reported by individual subjects, such computational approaches can thus directly associate mathematical models of individual behavior with individual brain states.

Psychiatric research is in crisis. While current classifications of mental disorders have multiplied and sparked a highly controversial debate on whether all such patterns of behavior actually constitute mental disorders, let alone diseases (Frances and Raven, 2013), major research agencies such as the National Institutes of Health have stopped supporting research that is oriented at such traditional disease classifications and instead suggest to focus on basic dimensions of mental disorders such as reward learning or working memory. Such basic dimensions of mental disorders are supposedly not confined to specific traditional disorders. Instead, they should constitute new research domains that play a role in the development of a multitude of illness expressions and stages. Proponents of this approach

claim that future research along these lines will require disease concepts and nosological classifications to be fundamentally reconceptualized (Insel et al., 2010).

There appears to be hardly any common ground between proponents of traditional disease classification systems on the one hand and researchers focusing on basic neurobiological mechanisms on the other: the first ones criticize that besides disorders such as dementia, neurobiological research has largely failed to help classify mental disorders in clinical situations; the latter claim that this failure is exactly due to an outdated way of looking at mental disorders. They suggest ceasing to classify mental disorders by key symptoms that have been handed down by generations of clinicians and instead suggest focusing on quantifiable models of human behavior and its underlying basic computational mechanisms.

Situations in which traditional certainties are questioned by modern research and in which the ensuing controversies appear to be fundamentally unsolvable have repeatedly been described in theoretical accounts of scientific development. For example, Kuhn (1962) suggested that "scientific revolutions" take place once established theories and the key paradigms on which they are built appear to be outdated: this is often the case when established paradigms have served their purpose; have helped to explain phenomena as best as they can; and scientists are becoming increasingly dissatisfied with the limits imposed by the established approaches to gaining further insights. Hence, new theories, which in many ways may be less elaborated than the traditional ones, will be tested, and scientists will start to use them exactly because they offer new insights, even if—at the present moment—they are overall less elaborate and useful than the traditional ones. In this respect, Fleck (1979) suggested that a key process in science is indeed learning by doing: by applying concepts and testing their usefulness, we learn to see the world through the eyes of such models; we understand where certain paradigmatic approaches and explanations can help, where they have to be refined, and where they are actually useless.

Thus, psychiatric research could be just at the point of such a scientific revolution—traditional concepts (although, as we will discuss, clinically useful and to date irreplaceable—will in the short or long run be replaced by new ways of looking at mental disorders. One of these ways is described in this book: a focus on basic learning mechanisms, which can be operationalized in computational models in order to better explain the development and maintenance of mental disorders. Basic learning mechanisms and the role they play in human behavior include Pavlovian conditioning; that is, the effects of Pavlovian conditioned cues on behavior (e.g., the

effects of a bell, which always rings when food is arriving, on saliva production in Pavlov's dog). They also include operant learning from feedback such as reward and punishment and the effects of Pavlovian conditioned stimuli on such instrumental, goal-directed behavior. Such basic learning mechanisms can help to describe how goal-directed behavior can be transformed with increasing practice into habits that are hard to modify by new rewards or conscious decisions (imagine how hard it can be to change a well-established but hurtful move in sports or dancing).

Focusing on such learning mechanisms has two advantages: first, it directly refers to key traditions in animal research and behavior therapy; namely, the study of behavioral effects of reward and punishment as well as the association between cues and reactions. Even more complex approaches in psychotherapy, such as psychoanalysis, have to some degree incorporated such ideas; for example, by focusing on the libido—desire or "wanting" of certain stimuli—or outcomes that motivate and drive decision making in living beings. A second advantage is that focusing on learning mechanisms not only helps to identify basic neurobiological mechanisms and their potential alterations in mental disorders but also allows emphasis of the variety and diversity of human behavior. Indeed, by identifying such basic learning mechanisms and providing a plausible and rational account of how they modify behavior, the resulting explanatory models of human behavior leave ample space for individual experience in the development and maintenance of mental disorders: on the one hand, such disorders can be promoted by basic alterations in learning mechanisms (e.g., an increased focus on negative outcome that can render subjective experiences gloomy), and on the other hand, exactly the same learning mechanisms are directly informed by personal experiences and hence social interactions. Indeed, learning from reward and punishment are two of the research domains suggested by the current research agenda of the National Institutes of Health (Insel et al., 2010).

Moreover, focusing on such basic dimensions has a much longer and more complex history, which includes attempts to map emotions by valence and arousal, resulting in at least two dimensions, one representing positive affect and ranging from highly arousing positive to boringly negative emotions, and the other charting negative affect, which ranges from highly arousing negative to boringly positive emotions (Crawford and Henry, 2004). Of course, philosophers such as Epicurus have long suggested that human beings strive to minimize pain and to maximize positive affect (Ingwood and Gerson, 1994). And the debate on whether human behavior is driven by such basic motivational forces or rather by rational insight has a

long-standing history in philosophy of mind and in philosophical anthropology. We will explore some of these traditions, not because they are interesting by themselves (what they are), but because some of these traditions can help to caution us not to rely on oversimplified models and because they may reveal aspects of human behavior that are otherwise out of sight. Thus, a main aim of this book is to explore how learning mechanisms and their currently identified neurobiological correlates help us to understand mental disorders. But before we further explore these topics, we need to define two concepts just mentioned: what are "mental disorders," and what do we mean when we talk about "understanding" them?

Let us start with the first topic, which has been the focus of considerable controversy during the past years. Like any field of research, psychiatry and its nosology were rather simple when modern scientific classifications were developed more than 100 years ago (figure 1.1). Basically, at this point there was a sixfold (three columns × two rows) distinction in place.

In the first column, disorders with a known organic cause were described and categorized according to whether this cause has an *acute* or a more

Exogenous psychoses (brain organic syndromes)	Endogenous psychoses	Variations
Acute e.g. delirium	The group of schizophrenias	Neuroses (trauma & conflict-related causes)
Chronic e.g. dementia	Major affective disorders (unipolar & bipolar depression)	Personality disorders (traits)

Figure 1.1
Traditional classification of mental disorders.

chronic impact on the brain. Basically, *acute* deliria and other forms of acute organic mental disorders (nowadays often called organic hallucinations, organic paranoia, etc.) were distinguished from more *chronic* forms of mental disorders such as dementia. The former often are associated with clouding of consciousness and disorientation, the latter with impairments of memory function. These disorders were called "organic" because, as in the case of Alzheimer's dementia, visible alterations were observed in brain anatomy (atrophy) and in the structure of cellular and intercellular space (fibrils and tangles). Deliria were called "organic" syndromes not because the exact biological correlates of, for example, delirium tremens were known, but rather because it was plausible that alcohol withdrawal has a direct ("organic") impact on the brain. These two major categories are still reflected in the main International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10), blocks F0 and F1 (World Health Organization, 2011).

In the second column, a fundamental distinction was put in place by Emil Kraepelin, who studied mental disorders that appeared to have a similarly devastating effect on human behavior as observed with the above listed "organic" brain disorders (although in his time, no definite organic cause was found by looking at postmortem brains). He distinguished between disorders that mainly interfere with affect and those that mainly impair cognition. Cognitive impairments were the hallmark of so-called dementia praecox (later renamed schizophrenia), and altered emotions characterized so-called manic-depressive illness (with depression limiting affective responses to the negative range and mania doing the same in the positive range). Here, Kraepelin followed the intuitive distinction between "thinking" and "feeling" and claimed that dementia praecox mainly displays a chronic, continual cause (with Kraepelin largely ignoring the negative effects of prolonged hospitalization of his patients without any treatment), while manic-depressive illness was supposed to follow a cyclic course of illness (Kraepelin, 1913, 1916). We will later focus more on current criticisms of this dichotomy, which is today still reiterated in the distinction between schizophrenia and bipolar disorder in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5, published by the American Psychiatric Association (2013), as well as in the major blocks F2 and F3 of the ICD-10 promoted by the World Health Organization (2011).

Finally, in the third column a major group of disorders was listed that were not really regarded as diseases (i.e., major mental disorders), but rather as "reactions" to common stress factors or "varieties" of human behavior. Such disorders included the effects of traumatic experiences as well as distinct

personality traits, nowadays classified as a variety of disorders including personality disorders and previously so-called neurotic disorders, which are currently grouped in ICD-10 under the blocks F4 and F6.

However, with all due respect to traditional and current disease classifications, do we really believe that all of these disorders constitute "diseases" in the medical sense? This question points to a discussion about the disease status of mental disorders, which was vivid during the reform of psychiatry in the 1970s and early 1980s. For example, Szasz (1970) criticized the medical disease concept of mental disorders and claimed that in the absence of clearly defined neurobiological correlates, which help to distinguish a mental disorder from a normal, healthy mental state, psychiatry does not describe diseases (with a potential exception of dementia) but instead sanctions social norms and falsely labels socially unwanted or unacceptable behavior as medical problems. Such criticism sparked a long-lasting controversy among medical philosophers, researchers, and clinicians. For the sake of clarification, it is helpful to review the distinction between the concepts of "disease," "illness," and "sickness." The medical aspect of any major malady is commonly called a "disease," the subjective experience contributes to the "illness" experience, and the impairment of social participation is usually called a "sickness" (Sartorius, 2010; Heinz, 2014). We and others have suggested that a clinically relevant mental malady requires the presence of medically relevant symptoms (thus fulfilling the disease criterion) as well as individual harm, which could either be due to a state of suffering from the aforementioned symptoms (the "illness" experience) or a severe limitation of social participation (as in the case of dementia, where a person may not subjectively suffer from memory loss but is unable to perform necessary activities of daily living such as personal hygiene or food intake). We thus conceptualize clinically relevant mental maladies as the combination of disease symptoms with either individual suffering (the illness experience) or impaired social participation (sickness). However, if we do so, a question arises: Which key symptoms of mental disorders can be regarded as medically relevant indicators of a disease and hence as necessary but not sufficient indicators of the presence of a clinically relevant mental malady?

In general medicine, a dysfunction is considered to be a symptom of a disease if it is relevant for individual survival; hence, being unable to roll your tongue, although being a genetically determined dysfunction, is no symptom of a disease, because rolling your tongue is irrelevant for survival. In contrast, being unable to swallow, another dysfunction of the tongue, is highly relevant for human life and is therefore rightly considered to be a symptom of a disease (e.g., a stroke or some impairment of cranial nerves).

Indeed, the medical philosopher Christopher Boorse (1976, 1977, 2012) suggested that in mental disorders, the disease criterion is fulfilled if functions are impaired that are relevant for individual survival. Boorse further suggested that functions relevant for procreation of the species should also be included among functions whose impairment indicates a disease; however, this latter proposal is highly controversial, as it may suggest that subjects who refrain from having children, have a sexual orientation toward their own gender, or have any other reason for decreased rates of procreation suffer from a mental disorder—a point that we and others have sharply criticized. Indeed, we strongly feel that medicine should focus on the health of the individual and abstain from forcing subjects to behave in a certain way in order to fulfill any perceived or constructed need of the "species."

But even if we limit our account of medically relevant functions to those necessary for individual survival, how can such functions be identified? Philosophers usually stop at this point and leave the further elaboration of such definitions to clinical practitioners, who often do not care about the proposals of their philosophical counterparts. Therefore, accounts of basic mental functions and hence of key symptoms indicating a potential mental disorder vary considerably. One way to solve this question, which we feel to be promising in this context, suggests to abandon theoretical construction of potentially relevant mental functions and instead to perform a "pragmatic turn" and to analyze whether key symptoms already used to classify mental disorders (figure 1.2) indeed describe impairments of mental functions generally relevant for human survival in multiple settings and situations. Doing so, it is easy to see that delirium tremens is characterized by clouding of consciousness and disorientation, two functions (consciousness, orientation) that are generally (universally) relevant for human survival. Indeed, it is easy to imagine a multitude of situations (e.g., crossing a road in New York or walking through a jungle in Borneo) in which clouding

1. Vigilance
2. Orientation: person/place/time
3. Understanding communication (including proverbs)
4. Concentration (100 – 7: repeatedly subtract 7 starting from 100)
5. Short-term memory (3 concepts/10 min.)
6. Long-term memory

Figure 1.2
Key symptoms to diagnose acute and chronic brain organic syndromes. Concentration is tested by, e.g., repeatedly subtracting the number 7 from 100.

7. Formal thought disorder (coherence, speed, subjective inhibition)
8. Delusions (delusional mood, delusional perceptions, systematic delusions)
9. Ego disorders (thought insertion, thought broadcasting, thought blockade)
10. Hallucinations (visual, acoustic, commenting voices, voices arguing, commanding voices)
11. Obsessions and compulsions
12. Mood (elevated, depressed, anxious, affective resonance, early morning depression)
13. Drive/motivation (reduced, inhibited)

Figure 1.3
Key symptoms of psychotic and affective disorders (e.g., schizophrenia and bipolar disorder).

of consciousness and disorientation can generally endanger the subject's life (remember that in order to diagnose a clinically relevant mental malady, such symptoms indeed need to cause individual harm, be it that the persons suffers from being disoriented or that she cannot perform activities of daily living such as contacting other persons, etc.).

The situation is more complicated when we look at the key symptoms that to date are used to diagnose schizophrenia or bipolar disorder (figure 1.3). While hallucinations may in general impair the ability of a human being to survive (imagine visual hallucinations that make it very difficult to walk through a room, let alone a city), many hallucinations occur at single time points and carry specific messages that do not directly cause disorientation or a general inability to behave in a given environment (e.g., voices commenting from time to time positively on a subject's performance). However, it can be very difficult to live in a common world with others once, for example, acoustic hallucinations include commanding voices that order a subject to attack someone else. If this subject is indeed following these orders and attacks another person, the attacked subject does not know whether this was a decision of the attacker or whether the attacker was just following the hallucinated orders. Likewise, if during a major depression a person is unable to feel joy (e.g., if her child or grandchild is born) or—in mania—is unable to feel grief even though her best friend has died, it will be very difficult to live in a common world with others. The key symptoms of our major medical disorders thus either directly jeopardize individual survival or (at least) impair basic activities in a world that is shared with

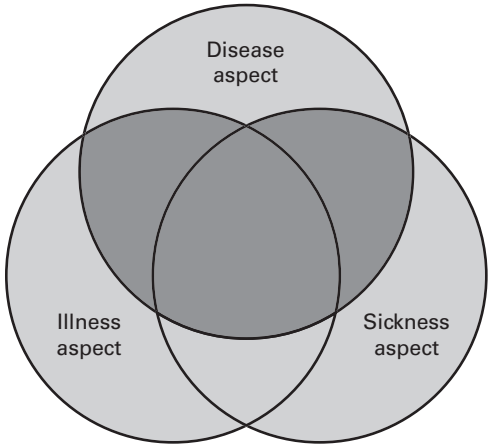

Figure 1.4
Concept of a clinically relevant mental malady. A clinically relevant mental malady (shaded area in this illustration) should only be diagnosed if medically relevant symptoms are present (the disease aspect of a mental malady, top circle) and either cause individual suffering (the illness aspect of a mental malady, lower left circle) or a severe impairment of activities of daily living and hence social participation (the sickness aspect of a mental malady, lower right circle). Therefore, only disorders located in the shaded area are diseases defined by medically relevant symptoms that have harmful consequences for the individual (suffering or severely impaired activities of daily living) and hence constitute clinically relevant mental maladies.

other human beings. However, the latter argument only holds if we assume that it is a key part of human nature to live with others (as we do). Then, functional impairments such as imperative voices or the inability to feel joy or grief can be counted as major dysfunctions, which constitute the medical aspect of a disease.

At this point, we would like to emphasize that the manifestation of a symptom of a disease, for example a hallucination, is not enough to diagnose a clinically relevant mental malady—the person also has to suffer from it or the hallucination has to impair basic activities of daily living (figure 1.4). One of our patients entered the hospital by stating that we should "leave his voices alone": "I speculate at the stock exchange, the voices tell me where to invest and so far their recommendations have always been useful!" In such cases (and in the absence of further symptoms, personal suffering, and an impairment of daily living), a doctor may well diagnose a medically relevant dysfunction (voices are acoustic hallucinations and

hence a disturbance of generally life-relevant perception), but—as we feel—the same doctor should abstain from diagnosing a clinically relevant mental malady, because the person reporting the hallucinations neither suffers from them nor is impaired in coping with her activities of daily living.

The resulting concept of a clinically relevant mental malady is, however, much narrower than all the behavior patterns classified in DSM-5 or ICD-10 as mental disorders. For example, it may be hard to argue why experiencing social phobia only when speaking in front of a major audience should be counted as an impairment of a medically relevant function that is generally relevant for human survival (or even for living with others in a common world)—there are, as we feel, many human subjects who are not able to give speeches in front of other people who are nevertheless able to live a satisfying life. On the contrary, this example shows that the empirical application of philosophical concepts always results in descriptions and definitions with "vague" boundaries: what at a certain point in time did not represent a mental function necessary for survival (or for basic interactions with others) may become so in the future (or even in contemporary society, given the abundance of PowerPoint presentations required to present yourself and your work in front of others). What we want to emphasize here is that mental disorders (such as social phobia manifesting itself when speaking in front of an audience) are a much broader category that includes multiple states of human suffering, which is why medical diseases (such as delirium tremens or bipolar disorder) are only a subgroup of such disorders characterized by their universally high relevance for human life. We indeed feel that medically relevant diseases should only be diagnosed if the functions impaired in such states (as indicated by key symptoms to diagnose the disease) are relevant for the individual person's survival or her basic ability to interact with others. It is open to public debate which exact functions should be classified as medically relevant, and medical doctors as well as psychologists have professional knowledge that helps to articulate such suggestions; however, the final decision is up to an open dialogue in society, which needs to include the views of patients and their relatives, lawmakers, and the broader public. In the current volume, we will focus on major mental disorders (i.e., such states that have traditionally been and in our view are rightfully called diseases: addiction, psychoses, and major affective disorders). However, while doing so we will touch on related phenomena such as anxieties and other negative mood states, cravings, obsessions, and experiences of alienation.

Finally, we need to discuss what we mean when we talk of "understanding mental disorders." As suggested earlier, modern computational tools

help us to analyze behavior on a much more complex level than previously possible. For example, such studies can use rather straightforward decision-making paradigms, in which you can press a left or right button and are rewarded probabilistically (i.e., in only 80% of all times once you press the currently better button), and after a while, unannounced switches will occur after which you have to learn the better choice again. As simple as this task may seem to be, it can be solved with a multitude of strategies: you can compute the feedback immediately after your choice (e.g., if you press the left-hand button you memorize the reward or punishment that follows your choice); alternatively, you can also compute the reward you *would have* gained if you *had* chosen the other option (the right button, which you did not press). Moreover, you can react more strongly to punishments (unexpected losses) than to rewards, which is a behavioral pattern that many individuals display. Finally, you can start counting in order to find out how many negative feedbacks have to occur to make it very likely that another unannounced change has occurred and you better switch your choices (in the above given example, it is now better to press the right-hand button, even though this choice was previously punished most of the time). On the basis of individual behavior patterns, researchers can build different mathematical models and find out which one of them can best explain the respective choices of the individual proband (more about that in later chapters). Understanding behavior with such computational tools hence means that you can analyze and model it. Furthermore, it suggests that human decision making may generally follow such mathematically describable patterns, which can be simulated by a computer and hence explained in mathematical terms.

However, understanding mental disorders traditionally had a much wider meaning: Dilthey (1924) suggested distinguishing between an *explanation* of behavior (e.g., in the above given example by mathematical models or, in his time, by assumptions about organic causes of behavior) and *understanding* human behavior, which requires some degree of empathy and relies on your personal experiences. To support his view, Dilthey suggested that if you want to learn something about human psychology, reading novels will have a much more profound effect compared to reading the results of experiments provided by the then-developing scientific psychology. What was true for the end of the nineteenth century to some degree still appears to be true in our contemporary times: the "how it is to be" aspect of any human behavior can easily get lost in mathematically articulated "computational" descriptions of human behavior. However, focusing on learning mechanisms and their modification of and by experience may, as we feel,

help to bridge the gap between a mathematical *explanation* and a subjective *understanding* of human behavior and its alteration in mental disorders: all people know how it "feels" to learn from experience, all have experienced rewards and punishments, received gains and suffered from losses, anticipated positive and negative outcomes, and went through hope and despair. As we will try to show in this volume, applying modern computational techniques to explain behavior does not mean to ignore subjective experience but rather to respect its uniqueness by trying to better understand how individual human experience is modified by learning mechanisms throughout the life span. Also, we want to emphasize that in spite of using computational techniques to explain human behavior, a human being, its body and its central nervous system, are much more complex than any computer simulation will ever reveal. Even if we focus on the central nervous system and its main organ, the brain, this living organ is in a dynamic interaction with a multitude of somatic inputs (e.g., from sensory organs, hormonal systems, etc.), which reflect states of the human body and its environment and represent extremely complex information in digital as well as analogous ways. If we want to identify computations performed by a brain by using in vivo imaging techniques and by simulating the decisive steps with our most advanced mathematical techniques, we look at just a minor part of all the rhythms and dynamics occurring in this organ. This remark should protect us from any kind of reductionism: science per se has to reduce the complexity of any given situation in order to find regularities that at best can be described using some mathematical formula or other ways to predict future events. We thus form a qualitative or quantitative (mathematical) model of our environment, which for the sake of parsimony is less complex than the facts in focus. However, trying to explain human behavior by using mathematical models and linking them with brain signals to help understand human experiences can reduce the complexity of these experiences without ignoring all that cannot be captured by such models: multifold and extremely diverse, valuable and highly important parts of human life uncharted by scientifically unavoidable, pragmatic reductions of complexity via experimental settings and paradigms.

The current volume will proceed in three parts. First, it will explain Pavlovian and operant conditioning, Pavlovian-to-instrumental transfer, and the distinction between habitual and goal-directed decision making (chapters 2–4). This part will help to illustrate and explain basic learning mechanisms and their respective effects on human behavior. Following a dimensional approach in psychiatry, our account will not focus on single disorders but rather explain basic mechanisms that are supposed to be at

work in a multitude of mental states and disorders. In the second part (chapters 5–9), we will explore how far such basic dimensions of mental disorders carry us when we try to explain key syndromes of mental disorders, such as craving and loss of control in addiction, positive and negative mood states in affective disorders, as well as experiences of being alienated with respect to one's own embodied self and the environment in psychotic states. Again, we will not focus on single distinct disease categories (schizophrenia vs. brief psychosis vs. schizoaffective disorders vs. psychotic experiences in organic hallucinations) but rather explain key mechanisms with respect to their syndromatic correlations. At the end of chapters 7–9 and in the last part of the current volume (chapter 10), we will explore clinical and therapeutic implications of such accounts. Computational approaches in psychiatry that focus on basic dimensions of human decision making, specifically on learning mechanisms, may thus offer a way to look at human diversity, emphasize personal experiences, and help to explain why not one mental disorder is effectively like another.

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