Chapter 11
Concluding Remarks: Where Do We Come From? Where Are We Moving To? Towards the Development of *Precision Psychotherapy*

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Abstract After our journey through the ongoing paradigm shift from a disorder-centred approach to a person-centred approach and then to a functional domains perspective, we introduce the RDoC framework as a current working model and research agenda to support this paradigm shift. Furthermore, we discuss how it orients the authors of each chapter of this book. After detailing the contents of each chapter, we discuss whether it is possible to define precision psychotherapy and determine its contributions to clinical work.

Keywords Functional domains · Precision medicine · Precision psychotherapy · Personality disorder · Depression

In daily clinical practice, we continue to employ a categorical approach to make mental health diagnoses and plan treatment delivery. For these diagnoses, we resort to the usual DSM/ICD criteria, since they have been used for decades in communications among professionals, at an administrative level, in research, and even to apply for funding, which until recently required DSM/ICD diagnoses to finance

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projects. As is well known, this approach derives from the Kraepelinian model, according to which mental disease is a discrete medical condition with clear boundaries between health and disease, and with clear diagnostic boundaries between disorders. In other words, the person either has a disorder – e.g. a personality disorder – or not (Trull & Durrett, 2005). It is further assumed that patients suffering from a disorder require treatment, whereas those not afflicted by one do not (Trull & Durrett, 2005). This approach was once applied to depression, which was largely regarded as a discrete, one-dimensional entity, and to personality disorders. Although this stance was comfortable, especially for clinicians, and even though it was designed to minimize uncertainty and sooth those who felt part of the "non-diseased", categorical diagnoses began to be challenged as early as the 1990s, particularly regarding personality disorders (Arbeitskreis OPD, 1996). Gradually, more and more critical voices echoed these views, drawing attention to the empirical unsustainability of the attempts to differentiate people with and without personality disorders in a categorical manner (Clark, Cuthbert, Lewis-Fernandez, Narrow, & Reed, 2017; Ehrenthal & Benecke, 2019; Haslam, Holland, & Kuppens, 2012; Zimmermann, 2014). Nowadays, authors largely suggest that personality traits are distributed within a continuum allowing for a gradual transition to pathological manifestations, as the evidence supports the existence of a range from normal and abnormal personality (Pukrop, Herpertz, Sass, & Steinmeyer, 1998; Trull & Durrett, 2005; Tyrer, 2020; Widiger, Simonsen, Krueger, Livesley, & Verheul, 2005).

The DSM-5 Alternative Model (American Psychiatric Association, 2013) is informed by these scientific advances; however, it preserves its traditional categories in the rest of its classificatory system. Interestingly, the authors focus on dysfunctions, noting that, in their alternative model, "personality disorders are characterized by impairments in *personality functioning* and pathological personality traits" (p. 761, our emphasis). This concept is also adopted in other classification systems and in the present book, as we will discuss later. Amid this knowledge milieu, the impact caused by the ICD-11 (World Health Organization, 2018) is worth noting. Its presentation and discussion, led by Jeffrey Reed at the 15th International Congress of the International Society for the Study of Personality Disorders (ISSPD) in Heidelberg, Germany, in September 2017, caused great controversy and heated reactions from the audience (Behn A., personal communication, 2017). The ICD-11 abolishes personality disorder categories, but defines a continuum that comprises personality difficulties, mild disorder, moderate disorder, and severe disorder, taking into account a set of dimensional constructs: emotional dysregulation vs stability, extroversion vs introversion, antagonism vs compliance, and impulsiveness vs repression. As we can see, this approach also represents a dimensional perspective informed by the assessment of functionality.

Research Domain Criteria (RDoC; Cuthbert, 2014, 2015), which see pathology "in terms of deviations in fundamental functional systems" (Cuthbert, 2014; p. 31), are the most radical contribution in this regard. RDoC, as described in other chapters of this book, is a "framework that is designed and intended to both foster and accommodate new research findings on a continual basis" (p. 30). It defines five domains of functioning that contain various constructs that can be studied or

described and enriched at multiple levels of analysis, ranging from the genetic and the molecular to manifest behaviour and self-reports. These functions are influenced by developmental and environmental factors.

According to RDoC and the accumulated empirical evidence, which increases day by day, human mental/cerebral/behavioural functioning can be evaluated relative to a normal curve: as it deviates from the curve, it becomes dysfunctional and constitutes a pathology. The RDoC is currently the most developed effort within a broader functional domains perspective. An interesting advantage of focusing on functional domains is the chance to develop relevant therapeutic targets within a single traditional diagnostic category. For instance, self-critical dysfunction and behavioural inhibition can be key therapeutic targets for depressive patients. Similarly, one functional domain dysfunction can work as a transdiagnostic therapeutic target so that interventions can have a transdiagnostic utility. For example, interventions to help improve emotional dysregulation can be useful for patients with borderline personality disorder comorbid with depression, or even in patients with anger control issues or mood dysregulation. This can lead to the development of modular treatments that can be eventually tailored to improve affected functional domains. This approach is addressed in the chapters of this book, of which we will highlight some examples below.

Approaching psychopathology and its treatment based on transdiagnostic dysfunctions brings us to the domain of precision medicine (Insel & Cuthbert, 2015). Developed in the oncology field, this concept indicates that, thanks to new insights into the biology and genetics of cancer, it is possible to indicate more effective treatments for specific manifestations of this disease. “In precision medicine, the focus is on identifying which approaches will be effective for which patients based on genetic, environmental, and lifestyle factors” (Genetics Home Reference, 2019). As is well known, mental health treatments are largely based on psychosocial interventions (psychotherapy); psychotherapy influences environmental factors and thus brain functioning across disorders (Barsaglini, Sartori, Benetti, Pettersson-Yeo, & Mechelli, 2014), including personality dysfunction (Gabbard, 2000; Mancke et al., 2018), which can be mediated by epigenetic factors (Jiménez et al., 2018). Therefore, and in line with the aim of this book, namely, to address psychopathology based on a functional domain perspective, we advocate for the application of precision psychotherapy to standard mental health care. In the words of Insel and Cuthbert (2015), “one of the most powerful and precise interventions to alter such (brain) activity may be targeted psychotherapy … which uses the brain’s intrinsic plasticity to alter neural circuits and as a consequence, deleterious thoughts and behavior” (p. 500).

The book’s introduction contextualizes the title of our book, “Depression and Personality Dysfunction: An Integrative Functional Domains Perspective” and provides a logic for the delivery of its contents. First, in line with the points made above, the book develops the idea that personality functioning includes relevant domains of functioning to be targeted transdiagnostically, including self and other functioning, self-criticism, affect dysregulation, reflective functioning, social dysfunction, meta-cognitive capacity, and identity regulation. In this context, we

express our preference for the term *personality dysfunction* instead of personality disorder. This distinction is quite relevant from a dimensional perspective and also acknowledges a continuum from healthy personality traits to sub-diagnostic threshold dysfunction and into the realm of full-blown personality pathology. In other words, it broadens the scope of clinically relevant deficits in functional domains integrated into the notion of personality functioning. The authors of each chapter work within this contemporary perspective while also incorporating the concept of complex depression, which reflects the multidimensionality of the depression diagnosis and its aetiology – discussed in another volume of this series – as well as the multiple factors that take place in the evolution, prognosis, and therapeutic response of this dysfunction. In the introductory Chap. 1, "Depression and Personality Dysfunction: Towards the Understanding of Complex Depression", the authors adopt the perspective of "functional domains that are differentially affected in depression concurrent with personality dysfunction and on personality styles as well as how the co-occurrence of both impacts on the severity of the condition" (p. 1 of the chapter). Interestingly, the authors stress the relevance of intermediate phenotypes, which underlie complex phenotypes such as depression and its interaction with personality. This approach would allow both understanding of common or differential underlying mechanisms to the respective phenotype and also enabling practitioners to suggest treatments focused on these intermediate phenotypes.

In Chap. 2, "The Functional Domain of Identity", part of Section I, "Domains of Personality Dysfunction Complicating the Presentation and Treatment of Depression", the authors present an in-depth discussion of identity dysfunctions, addressing their role not only in personality disorders but also in depression, with which they have a bidirectional relationship: doubts about one's identity can cause depression and early depression can have an impact on identity development. The authors show how the concept of identity is relevant for understanding the comorbidity between depression and the so-called borderline personality disorder (BPD). They take chronic emptiness to be a manifestation of both depression and BPD and assert that as long as this dysfunction (which could be regarded as an intermediate phenotype) remains untreated, neither depression nor personality dysfunction will show any improvements. Chapter 3, "The Functional Domain of Affect Regulation", presents a detailed exchange and discussion with the RDoC model, understanding affect regulation "as a mechanism that lays at the crossroads of several of the systems proposed by the RDoC" (p. 4 of the chapter). The authors propose a developmental approach based on attachment theory and developmental research in which affect regulation constitutes a fundamental element of self-development, with this function being linked to the RDoC dimensions "social processes" and "arousal/regulatory systems". Chapter 4, "The Functional Domain of Self-Other Regulation", operates as a continuation of the previous chapter: the authors present a model for understanding this functional domain (and its dysfunction) as a result of the interaction of three systems: stress regulation (negative valence system + arousal/modulatory systems), reward (positive valence systems), and mentalizing systems (systems for social processes). These two chapters rise to the challenge of meeting the recommendations of the RDoC initiative in order to understand each functional domain/

dysfunction, including developmental trajectories and environmental effects, especially with respect to the pathogenic role of adversity in childhood. Chapter 5, "The Domain of Social Dysfunction in Complex Depressive Disorders", focuses on the units of analysis of the "behaviour" and "self-report" of the RDoC model and describes how five domains of this dysfunction manifest themselves in various types of complex depression. The authors assert that treatment must address both depressive symptoms and functional improvements, that is, this approach operates at the level of phenotypic expression. In Chap. 6, "Neurobiological Findings Underlying Personality Dysfunction in Depression: From Vulnerability to Differential Susceptibility", after examining the personality-depression link and elaborating on the neurobiology of personality traits in this disorder, the authors address gene-environment correlation and gene-environment interaction. The authors cover a range of topics from RdoC genetic levels of analysis to the phenotypic expression of environment susceptibility. The authors confirm the points made thus far: "there is now increasing consensus that most common psychiatric disorders, such as depression and anxiety, are best explained as complex disorders involving dysfunctions in several biological systems in interaction with environmental factors" (p. 14, Chap. 6). The section concludes with Chap. 7, "The Functional |Domain of Self-Criticism", whose authors conduct a detailed examination of this domain of functioning, described as an aberration in depression and/or personality dysfunctions. This is a good example of how the construct can manifest itself "normally" or reach pathological and self-destructive levels. The situation becomes more complex after interaction with the moderating effect of personality structure, with more vulnerable personality structures exhibiting more pathogenic self-criticism. The authors also show how different therapeutic approaches can deal with the same dysfunction, in this case, one of a self-critical nature.

In Section II: "Integrative Models of Depression and Personality Dysfunction: Implications for Diagnosis and Treatment", the first two chapters address complex depression. In Chap. 8, "Complex Depression and Early Adverse Stress: A Domain-Based Diagnostic Approach", after reviewing the factors that increase depression complexity, the authors discuss the role of childhood adversity in depressive pathology, taking into account its manifestations, complications, prognosis, and treatment. Based on their own research, they propose a model aimed at differentiating complex depression from non-complex depression. Chapter 9, "Complex Depression in High-Pressure Care Settings: Strategies and Therapeutic Competences", addresses complex depression and its underlying dysfunctions, focusing on environmental factors. The authors link complex depression with the concept of *difficult patient*, noting that an adverse environmental context plays a key role regarding not only the patient's dysfunctional manifestations but also the practitioner's therapeutic capabilities and his/her relationship with the patient. The chapter offers multiple therapeutic approaches to specific personality dysfunctions. Chapter 10, "Modular Treatment for Complex Depression According to Metacognitive Interpersonal Therapy", offers a clear example of the therapeutic approach based on tackling specific dysfunctions that underlie the clinical manifestation (intermediate phenotype). The authors detail specific modules aimed at treating specific dysfunctions in order

to alleviate depressive symptoms and/or manifestations of personality structure vulnerabilities, representing a clear example of transdiagnostic treatments.

A look at the chapters of this volume reveals certain building blocks of knowledge that, apart from contributing to clinical work, help to ground future research. These building blocks provide several insights: that development results from the interplay of developmental tasks, relatedness, and self-definition; that alterations in this balance lead to different susceptibilities to environmental stressors that generate depression, causing self-critical dysfunction (which can be treated in a number of ways); that there seems to be crossed aetiopathogenesis between personality dysfunctions and depression; that childhood adversity is a critical factor in people's lives that makes them vulnerable to several pathologies (a vulnerability that has been decanted into a single "p" factor) (Caspi et al., 2014); that therapeutic interventions focused on mechanisms (intermediate phenotype) can generate symptomatic responses in depression and personality functioning; and that paradigms in the last few years have shifted from a disorder-centred approach to a person-centred approach and then (nowadays) to a dysfunction-centred approach. The latter approach, based on the insights presented in this book, can be referred to as *precision psychotherapy*. Nevertheless, in the psychotherapy field, the concept of precision medicine can be nuanced: the association between an altered functional domain and the therapeutic approach adopted, as noted above, is not univocal. Many examples can be presented of how a single dysfunction, self-criticism, emotional dysregulation, depressive inhibition, or identity diffusion could be successfully addressed with a variety of approaches. How can we account for this phenomenon? Does each strategy target a variety of unknown, unrecorded intermediate phenotypes that underlie measurable phenotypes, which is where we are recording a change? Future comparative studies might yield more information about intervention accuracy.

The clinical relevance of the RDoC initiative has been disputed in the literature (Carpenter Jr, 2016); however, the approaches presented in this book have all consistently taken into account the clinical perspective. Thus, specific tools such as those discussed here should inform the work of clinicians, who will apply them following the principles of evidence-based practice (American Psychological Association, 2005). As is well known, evidence-based practice rests on three pillars: best available evidence – e.g. some of the guidelines presented in this book – clinician expertise, and patient characteristics, culture, and preferences. In this regard, evidence-based practice presupposes some form of personalization, namely, the balancing of best available evidence with the personal characteristics of the patient, the therapies, and the context in which treatment is delivered. Treatment indication will result from a collaborative decision-making process involving the therapist and the patient (Mulder, Murray, & Rucklidge, 2017), in which the subjectivity of the latter and the possibility of establishing a therapeutic alliance are essential. No specific intervention will have an effect if it is not sown in the fertile ground of a good therapeutic bond, which in all likelihood requires personalization and not the robotic delivery of treatment manuals. In this regard, some problems remain underdeveloped. First, a precision psychotherapy model will heavily rely on the assessment of

affected deficits in functional domains. It is yet not clear how to accomplish this, mainly because most evidence-based assessment is geared towards the detection of standard psychopathology and not underlying, transdiagnostic deficits in functional domains. In this regard, the development of broadband measures to capture such deficits is key and can be aided by the use of state-of-the-art adaptive testing technologies. It is clear that even though conceptually sound, the clinical effectiveness of personalized psychotherapy is strongly contingent on the precision and practicality of the initial assessment of functional domains. Following this difficulty, precision psychotherapy requires the development of modularization, that is, the structuring of sets of interventions that target deficits in specific functional domains or intermediate phenotypes. This framework is also conceptually sound, but its implementation poses significant challenges, including the construction of modules, the design of specific delivery algorithms for modules (i.e. what comes first), the specification and creation of sensitive outcome measures to evaluate incremental progress on each functional domain, and, surely, profound changes in clinical training. Furthermore, some questions remain with respect to the role of the relationship in therapeutic change: is it always a moderating factor, or is its mediating effect on change scientifically demonstrable? The practitioner's ability to establish a bond with the patient – whom he/she will try to understand upon the basis of the patient's subjectivity, his/her own expertise, and empirical evidence – will depend on his/her practical wisdom (Jiménez & Botto, 2020). It is our hope that this book will enrich this practical wisdom from a scientific perspective.

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