Out of the box : moving from categories to dimensions in the phenomenology of depression and anxiety.

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CHAPTER 1

INTRODUCTION

This thesis focuses on the phenomenology of depression and anxiety disorders, and pleads for a transition from a categorical to a multidimensional approach in the description of these disorders.

The relationship between depression and anxiety disorders has drawn much attention for several decades. This continuing interest is mainly due to the high comorbidity between the disorders, and the similarities between effective treatments. In line with that, there is an on-going discussion about whether depression and anxiety disorders should be considered as separate diagnostic entities with specific phenomenological and neurobiological characterizations, or should be considered as manifestations of the same disorder.

The way the phenomenology of these disorders is described influences the design and the results of studies on the cause and treatment of the disorders. Although the development of clear categorical diagnostic criteria, as described in the widely used diagnostic system of the DSM-IV (Diagnostic and statistical manual of mental disorders (American Psychiatric Association, 1994, p. 111)), has advanced the field considerably, it has become more and more clear that a mere categorical approach hampers further progress. In this dissertation we set out to make a step forward from the use of categorical conceptualization to a dimensional approach of depression and anxiety.

In this introduction we first present the advantages and disadvantages of categorical systems. Second, we describe the general benefits of a dimensional approach, and present several dimensional approaches that have been proposed in the literature. Third, we discuss the tripartite model (a well-known dimensional approach) at length, and present some of the criticism on this model. Fourth, we explain how the tripartite model can be improved. Finally, we describe the main purpose and outline of this thesis.

1.1 Categorical systems

Categorical systems: advantages

In psychiatry the DSM-IV and ICD-10 (International Statistical Classification of Diseases and Related Health Problems) are the commonly used categorical sets of criteria for psychiatric diagnoses. Each disorder is defined by its symptoms and criteria are given which have to be met, for a diagnosis to apply. As an example the DSM-IV criteria for a Major Depressive Episode are shown in textbox 1.1.

The development of clear diagnostic criteria has advanced the field considerably. Since the introduction of the DSM and ICD, communication among professionals and among researchers about disorders and individual patients has become more straightforward. On top of that, comparing research results (e.g. in reviews and meta-analyses) has become much more effective and accurate.

DSM-IV criteria for Major Depressive Episode

Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood, or (2) loss of interest or pleasure.

1. Depressed mood (either subjective report or observation)
2. Markedly diminished interest or pleasure in activities
3. Significant weight loss when not dieting or weight gain
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation nearly every day
6. Fatigue or loss of energy
7. Feelings of worthlessness or excessive or inappropriate guilt.
8. Diminished ability to think or concentrate, or indecisiveness.
9. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or specific plan.

Textbox 1.1

Categorical systems: drawbacks

As a basis for research into psychopathology (e.g. endophenotype, genotype, trauma's, personality), a categorical approach has serious drawbacks. One problem with a categorical diagnostic system is the arbitrary nature of its diagnostic boundaries. For instance, the presence or absence of just one symptom can make the difference between meeting and not meeting the diagnostic criteria for a disorder. Indeed, research into etiological or risk factors for mental disorders shows that subsyndromal cases are very similar to cases fully meeting the diagnostic criteria for the disorder (McGorry, Hickie, Yung, Pantelis, & Jackson, 2006; De Beurs et al., 1999).

Another problem with categorical diagnostic classification is that patients with different symptom profiles may nevertheless meet criteria for the same diagnosis, which results in heterogenic groups of patients within a diagnostic class. To illustrate the heterogeneity of patients with a depression, we describe and compare the psychopathology of two patients in textbox 1.2. Both patients meet diagnostic criteria for a Major Depressive Disorder (MDD) according to the DSM-IV.

Although both patients fulfil the criteria of a MDD, they display a very different pattern of symptoms. This is possible because in the DSM-IV fulfilling five out of nine criteria described for MDD (see textbox 1.1), is enough to be eligible for a diagnosis. On top of that, several criteria contain both the increase and the

Two patients with Major Depressive Disorder (MDD)

Patient A (female, 36 years of age) is feeling sad and worthless, has problems with falling asleep, and has lost weight. She is quite agitated, is feeling very guilty towards her family (husband and two young children), and often wished she would not wake up the next morning ("that would be better for everyone").

Patient B (female, 29 years of age) does not enjoy her life as much as she used to do. She feels bogged down and sluggish. She sleeps a lot and has energy loss, gained 5 kilograms in the past 3 months and does not get anything done and can't concentrate.

Textbox 1.2

decrease of certain behaviour (e.g. weight loss OR weight gain). This illustrates that a group of patients with MDD may indeed be very heterogeneous group.

To complicate matters further, in the current diagnostic systems it is quite likely that a psychiatric patient meets criteria for two or even more, psychiatric disorders simultaneously. In fact, the majority of patients meet criteria of more than one psychiatric disorder concurrently (e.g., Brown, Campbell, Lehman, Grisham, & Mancill, 2001; De Graaf, Bijl, Smit, Vollebergh, & Spijker, 2002; Kessler et al., 1996). This is certainly true for mood and anxiety disorders (e.g., Belzer & Schneier, 2004). High rates of comorbidity between anxiety disorders and depression have been reported in the general population (Kessler et al., 1996), in primary care (Roca et al., 2009) and in secondary care (Brown et al., 2001).

As a syndrome is defined as a permanent combination of symptoms, it can be concluded that DSM-IV diagnoses are not real syndromes. Rather, they are more or less arbitrarily constructed clusters of symptoms. The etiology and pathophysiology of depression and anxiety disorders are unknown, and illness-specific treatments are absent. For instance, a wide range of emotional disorders respond similarly to the same psychosocial and psychotropic drug treatment (Brown & Leyfer, 2009). In this respect, the growing number of disorders in each new version of the DSM has led to questions about the discriminant validity of the categories. For example, the DSM-II had only three anxiety disorders (American Psychiatric Association, 1968) and the more recent DSM-IV includes twelve anxiety disorders (American Psychiatric Association, 1994). The distinction between these various anxiety disorders is predominantly based on their symptomatic phenomenology and not on established knowledge

regarding their etiology or treatment response to different (pharmacological or psychotherapeutical) agents.

1.2 Multidimensional models

General benefits of a dimensional approach

Many researchers and clinicians agree that the fields of psychiatry and clinical psychology could benefit from a dimensional model of the psychopathology of common mental disorders (Clark, 2005; Cuthbert, 2005; Krueger, Watson, & Barlow, 2005). A multidimensional model provides each patient with a symptom profile on a number of dimensions of psychopathology, rather than a dichotomous presence or absence of one or more disorders. It offers a more specific and accurate description of individuals, covers the full range of severity from healthy to severe psychopathology and may help to avoid stereotyping. Moreover, a multidimensional approach has the potential to associate psychopathology more accurately to etiological factors and biological markers and may predict more accurately which patients will benefit from a specific treatment (Kupfer, 2005; Widiger & Samuel, 2005).

The idea that a dimensional model has great benefits over a categorical system has gained much support in the last decades. Several dimensional models of depression and anxiety have been proposed. However, there is yet no clarity about which model is to be preferred. Among the models proposed so far, a distinction can be made between 'disorder-based models' and 'symptom-based models'.

Disorder-based models

There are several disorder-based approaches. The first line of research focuses on finding dimensions with optimal ability to discriminate between DSM patient groups, for example between generalized anxiety disorder and depression (Kessler et al., 2002; Wittchen et al., 2002). In this approach, the goal is to determine the symptom group(s) that represent(s) the most characteristic features of a DSM diagnosis.

A second disorder-based approach that is often referred to as a dimensional approach is the clustering of DSM-categories in a hierarchical way, with the aim to find common and distinctive features among various disorders based on their co-occurrence. In two large studies in respectively the United States (National Comorbidity Survey) and The Netherlands (NEMESIS study) the latent structure of common mental disorders was studied in the general population (Krueger, 1999; Vollebergh et al., 2001). In both studies the results of confirmatory factor analysis show an optimal fit for a hierarchical three-factor model, in which the internalizing problems are represented by two latent factors: 1) anxious misery (major depression, dysthymia and generalized anxiety disorders), and 2) fear (the other anxiety disorders). The third factor in these two studies

represents respectively the external disorders (Krueger, 1999), and alcohol/drug dependence (Vollebergh et al., 2001). For future research on common mental disorders both studies suggest to focus on core processes and core psychological features of the disorders, rather than on their manifestations as distinguished disorders, and on further differentiating between subtypes of disorders.

Referring to the studies of Krueger and Vollebergh, Watson states that "there are now sufficient data to eliminate this rational system and replace it with an empirically based structure that reflects the actual similarities among disorders" (2005). With 'this rational system' Watson means the DSM-IV, and he subsequently makes a suggestion for the structure of emotional disorders in the next version of the DSM, the DSM-5. He suggests to use a quantitative hierarchical model in which the mood and anxiety disorders are taken together to form an overarching class of emotional disorders with 3 subclasses (distress disorders, fear disorders and bipolar disorders) (Watson, 2005).

Although practical and intuitive, a disadvantage of this disorder-based approach is that the 'dimensions' are broad latent variables of existing DSM-IV categories, which are arbitrary and heterogeneous as discussed above. This means that the problems with a categorical system (arbitrary boundaries, comorbidity and heterogeneity of patient groups) are not fully resolved and seep into the new system.

Symptom-based models

A symptom-based dimensional approach is characterized by exploring large symptom-pools for underlying constructs, without requiring that the studied subjects meet particular DSM-IV diagnoses. This line of research focuses on the constructs of anxiety and depression and their overlap (e.g. Nitschke, Heller, Imig J.C., McDonald P., & Miller, 2001). The goal of these studies is to find dimensions that assess the relevant and distinguishable aspects of the psychopathology of mental disorders, commonly seen in outpatient care. In this line of research the DSM categories do not play a role in validating the constructs, and therefore the main advantage of this approach is that it can circumvent or bypass the problems inherent to the DSM-IV.

With psychometric techniques such as exploratory and confirmatory factor analysis, the structure of latent factors that underlie the symptoms can be explored. The discovered factors could be regarded as symptom dimensions. With respect to depression and anxiety disorders (the focus of this thesis), several dimensional models have been developed. An important contribution was made by Clark and Watson with the introduction of the tripartite model (Clark & Watson, 1991). In the next paragraph (1.3) the tripartite model will be described and discussed.

1.3 The tripartite model

Description of the tripartite model

Clark and Watson introduced the tripartite model to assess and model distinct and overlapping features of mood and anxiety disorders (Clark & Watson, 1991). This symptom-based model was initially proposed to explain the high comorbidity rates of depressive and anxious disorders. The first dimension is negative affect (NA). NA is characterized by aversive emotional states, such as being distressed, fearful and nervous, and is regarded as common to both mood- and anxiety disorders. The second is positive affect (PA) and contains 'enthusiasm, excitement and energy'. A low score on this dimension is typical for depression. The third dimension is 'somatic arousal' (SA) and is specific for anxiety.

The Mood and Anxiety Symptom Questionnaire MASQ

Clark and Watson designed a 90-item instrument to measure the three dimensions of the tripartite model, the Mood and Anxiety Symptom Questionnaire MASQ (Watson & Clark, 1991). Although the model consists of three dimensions (PA, NA and SA), the items of the MASQ are allocated on five subscales; in the proposed structure of the MASQ, Watson and Clark divided the dimension NA of the tripartite model into three subcategories: General Distress Depression, General Distress Anxiety and General Distress Mixed (see Figure 1.1). The items were assigned in line with their similarity with DSM-IIIR criteria for mood or anxiety disorders (American Psychiatric Association, 1987). All 90 items are presented with a five-point Likert scale ranging from 1 (not at all) to 5 (very much).

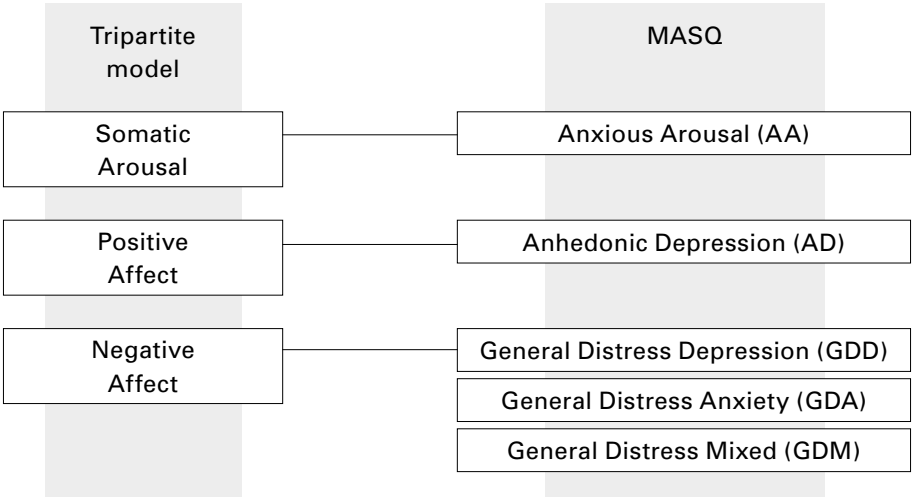

Figure 1.1 The tripartite model and the Mood and Anxiety Symptom Questionnaire.

Critique on the tripartite model

The tripartite model has inspired a large body of research, but has met some criticism as well. We will review the major points of critique on each of the three factors of the tripartite model and the MASQ.

First, there is criticism on the general distress factor NA. According to the theory of the tripartite model one would expect comparable relationships between NA and each of the different mood and anxiety disorders. However, large differences are found (Brown, Chorpita, & Barlow, 1998). This may be explained by the heterogeneous nature of NA. In the tripartite model, NA is characterized by aversive emotional states, such as feeling upset, angry, guilty, afraid, sad, scornful, and disgusted. Because the factor NA contains all these different constructs, it may be too heterogeneous to be regarded as a unidimensional construct (Shankman & Klein, 2003). With the proposed structure of the MASQ, Watson and Clark already acknowledged the heterogeneity of NA, as they divided the general distress items into three subcategories (See Figure 1.1). These three subscales of NA, however, were not confirmed with factor analysis of the MASQ-data (Boschen & Oei, 2006; Buckby, Cotton, Cosgrave, Killackey, & Yung, 2008; Burns & Eidelson, 1998).

Second, the PA scale is presented as a dimension with two endpoints: a low positive affect endpoint (lack of interest) and a high positive affect endpoint (feeling good). This assumption of the tripartite model that PA comprises of a single dimension with two extremes (lack of interest and feeling good) has however not been confirmed in analyses. Several studies showed that these two elements appear as separate factors in factor-analysis, suggesting that the two constructs do not belong to a single dimension (Keogh & Reidy, 2000; Nitschke et al., 2001; et al., 1995). Other evidence that lack of interest and feeling good are separate constructs is found in the research of Tomarken (2004). He reported medication to have a differential effect on lack of interest and on feeling good. Items assessing the low positive affect pole of the anhedonia dimension were more sensitive to earlier/lower dose bupropion SR treatment, whereas items assessing the high positive affect pole were more sensitive to later/higher dose bupropion SR treatment.

Finally, there is criticism on the third scale: somatic arousal. Although the model suggests a high score on SA is characteristic for all anxiety disorders, this is not the case, since it predominantly entails the symptoms of a panic disorder, such as increased heartbeat, transpiration, respiratory en gastro-intestinal symptoms (Chorpita & Daleiden, 2002; Joiner et al., 1999; Mineka, Watson, & Clark, 1998). Other types of anxiety symptoms like fear and worrying are therewith not well represented in the tripartite model.

The critics described above are largely focussing on the conceptualization of the tripartite model by means of the MASQ, and not on the model itself. The tripartite structure of the model is confirmed in many studies in different

populations (Bedford, 1997; Reidy & Keogh, 1997; Watson et al., 1995), and PA and NA are broadly accepted as a useful representation of affect, and being the dominant dimensions of self-reported mood (e.g., Watson, Wiese, Vaidya, & Tellegen, 1999; Remmington, Fabrigar, & Visser, 2000; Russell & Carroll, 1999). Therefore, despite the critics, the tripartite model is a strong basis for future research.

1.4 Extending the tripartite model

The current challenge is to develop a more refined model of phenotypes of psychopathology of depression and anxiety disorders, than the tripartite model. Although the tripartite model has met much support, we mentioned that it does not cover all relevant anxiety symptoms and that its negative affect dimension is rather unspecific. It is worthwhile trying to extend the tripartite model and move away from the DSM-IV. This is in concordance with the suggestions made by the original developers of the tripartite model. They proposed to specify the nature of unique components of mood- and anxiety disorders more precisely in a future model. In addition, they suggest to *"view individual disorders as representing unique combinations of different types of symptoms, with each type showing varying degrees of nonspecificity and with no type being entirely unique to any single disorder"* (Mineka et al., 1998).

Subsequently, we believe that in an ideal integrative approach, each dimension should cover a separate construct, and together the dimensions should assess the main aspects of the psychopathology of both depression and the specific anxiety disorders. The constructs should be unidimensional, have low intercorrelations, and together provide each patient with an accurate symptom profile. For instance, the two patients introduced in Textbox 1.2 would each have a different profile, despite the fact that both meet the criteria of the same DSM-diagnosis. With a specific symptom profile for each patient, more justice would be done to the idiosyncrasies of individual patients and their symptoms. Moreover, a dimensional model has the potential to associate psychopathology more accurately to etiological factors and biological markers. The ultimate goal is to improve our understanding of common mental disorders. A better understanding consequently may enable us to devise better treatments and ultimately may make it possible to predict which patients will benefit from a specific treatment for their complaints.

In this dissertation we take a step forward from the use of categorical diagnostic systems towards a dimensional approach of the psychopathology of depression and anxiety disorders. Towards this goal, several steps have to be taken. A first condition was the availability of large data sets from representative clinical samples to perform the analyses on. Until now, much of the research on dimensions of psychopathology has been undertaken with inappropriate samples such as college students or homogeneous patient groups, selected

to partake in clinical trials. Data on real life patients groups are much needed. In the spring of 2002, the Department of Psychiatry of the Leiden University Medical Center (LUMC) and the mental health institute 'Rivierduinen' (together serving a region of more than 1 million people), started collaboration for routinely assessing diagnosis and complaints at intake, and at 3-4 months intervals during treatment. The method is called Routine Outcome Monitoring (ROM). The data collected through ROM were available for this project.

The second step was to construct a Dutch translation of the MASQ, and to investigate its psychometric qualities and the fit of the tripartite model in our Dutch patient samples.

The third step was to expand the tripartite model in order to overcome some of the disadvantages of the tripartite model. Specifically, to cover anxiety more adequately additional anxiety-like constructs (e.g. phobic fear and anxious apprehension) had to be incorporated in the symptom-based dimensional model. On top of that, the statistical unidimensionality of factors had to be determined to guarantee that there were no heterogeneous dimensions in the model. We tested the applicability of various extended multidimensional models in a large set of data of psychiatric patients.

1.5 Outline of the studies

The data used for the analyses in this thesis, are collected in daily clinical practice by Routine Outcome Monitoring (ROM). Chapter 2 describes ROM as it was implemented in Rivierduinen and the LUMC in Leiden and presents data of the patient group included.

Chapter 3 describes a study into the relationship between comorbidity and severity. The aim of the study was to determine in a large outpatient sample whether patients with comorbidity have increased symptom severity and greater functional impairment as compared to patients with only a depressive or an anxiety disorder.

Chapter 4 reports on the psychometric properties of the Dutch adaptation of the Mood and Anxiety Symptom Questionnaire (MASQ). The Dutch version was constructed, its reliability and validity were tested, as was the fit of the tripartite model in our Dutch patient sample.

In Chapter 5 a proposal for an extension of the tripartite model is presented. The aim of this study was to develop scales that assess symptoms of depression and anxiety, that can adequately differentiate between depression and anxiety disorders, and that also better account for the diverse phenomenology of the various anxiety disorders.

With the study described in Chapter 6, we aimed to integrate aspects of several models into one broad dimensional model, that does not take DSM-IV diagnoses as a point of departure. The intended result was a multidimensional model to characterize patients in terms of their specific symptom profile, which

has potential for both clinical diagnosis and for use as a clinical phenotype.

Chapter 7 summarizes the main findings, provides a general discussion of these findings, and presents implications for theory, future research, and clinical practice.