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Diagnosing depression

1.1 Diagnosing and classifying

A diagnosis is the definition of a disorder as to its nature and seat. ‘Nature’ refers to its phenomenology, a etiology and course; ‘seat’ to the underlying pathophysiology. Diagnosing is the process leading to a diagnosis. In classifying a disorder all diagnostic considerations are condensed in a single construct that receives a particular code according to the taxonomy in force.

Classification systems are by no means ‘neutral’, noncommittal. They influence the way disorders are being diagnosed. One is inclined to steer the diagnostic process in such a way as to arrive at a diagnosis that fits the prevailing taxonomy. The impact of classification systems on diagnosing is the more pronounced the more detailed the diagnostic criteria are spelled out. The DSM system is a typical case in point. Diagnostic criteria are stated in great detail and hence the influence of that system on psychiatric diagnosing has been enormous. Diagnoses, so to say, are made with a copy of the DSM (Diagnostic and Statistical Manual of Mental Disorders; DSM–IV: American Psychiatric Association, 1994) in one’s hand, or at the least in the back of one’s mind.

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Basically, there are three ways to characterize psychiatric disorders, in this case depression: the nosological or categorical, the syndromal and the dimensional/functional approaches.

1.2.1 The nosological approach

The nosological disease model conceives psychiatric disorders as discrete entities, each characterized by a particular symptomatology, course, outcome and, at least in principle, a particular pathophysiology. In principle, because so far little is known about the neurobiological underpinnings of abnormal behaviour.

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This approach has dominated psychiatric diagnosing and classification since Kraepelin's days. Until 1980 nosological systems were not standardized and diagnostic criteria insufficiently spelled out. Many such systems were in circulation but none of them was internationally accepted. Moreover the various taxonomies were based on different criteria, such as aetiology, symptomatology, course and premorbid personality structure, each separately or in various combinations. The status of psychiatric diagnosing was chaotic and empirical research, based as it necessarily is on precise and standardized definition of the object of study, was thus virtually impossible.

In 1980, with the introduction of the third edition of the DSM, this situation changed dramatically. A detailed and standardized taxonomy of mental disorders was introduced in which the diagnostic criteria were carefully defined. It was solidly based on nosological principles. The system was embraced almost immediately by clinicians and researchers alike. The International Classification of Diseases (ICD) composed by the World Health Organization (WHO), a few years later, in its tenth edition, followed suit and introduced a system comparable to the one proposed in the DSM-III. Its impact on psychiatric diagnosing, however, remained modest compared with that of the DSM system.

1.2.2 Problems inherent to nosological systems

Nosological systems are by definition rigid, particularly so if disorders are characterized on a number of axes, and the defining criteria are specified in detail, as is the case in the DSM system. Patients have to meet all criteria to qualify for a particular diagnosis. Clinical realities, however, refuse to follow suit. In practice many patients are seen that do not meet all criteria required, and thus cannot be properly diagnosed and classified. This creates the need for an ever-increasing number of new diagnostic categories, at least if one wants to avoid overloading the categories 'not otherwise specified'. According to Pincus *et al.* (1992) over 150 new disorders were proposed during the DSM-IV process. The class of mood disorders is a case in point. In 1980 we started out with two main categories of depression, i.e. major depression and dysthymia. In the meanwhile a variety of new constructs have appeared, such as subsyndromal depression, atypical depression, brief recurrent depression, mixed anxiety-depression disorder, double depression and depressive personality (Angst *et al.*, 1990; Klein, 1990; Zinbarg *et al.*, 1994; Judd *et al.*, 1994, 1997; Hellerstein & Little, 1996; Herpertz *et al.*, 1998). In terms of aetiologically and phenomenology, no discontinuity has been demonstrated between those subtypes (Van Praag, 1997, 1998; Ormel *et al.*, 2001). In terms of symptomatology, course, outcome and treatment response, moreover, all those constructs show a fair degree of heterogeneity. Hence, their validity is modest at best. No doubt they show utility in clinical practice,

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as Kendell & Jablensky (2003) stressed, because they provide psychiatrists with a common language. For research purposes, however, they are an unsuitable starting point (Van Praag, 1997).

Particularly, the area between distress and depression has witnessed a plethora of new, so-called subthreshold entities (Sherbourne *et al.*, 1994; Olfson *et al.*, 1996). Subthreshold depressions are defined as conditions ‘that do not meet the full descriptive criteria for a specific mood disorder’ (e.g. having fewer than five out of the nine symptoms mentioned in the definition of major depression) but meet the ‘clinical significant criterion for DSM–IV’ (i.e. having clinically significant distress or impairment associated with them) (Pincus *et al.*, 1999). These conditions are distinguished from ‘subclinical’ conditions, in which individuals may manifest symptoms of a mental disorder, but the symptoms do not generate clinical distress or impairment (Roy-Byrne *et al.*, 1994). Taking into account that distress, used in opposition to depression, per definition generates indisposition, just as depression does, and no criteria are provided to distinguish ‘clinically significant’ from ‘clinically nonsignificant’ distress, this type of descriptive psychopathology represents diagnostic hair-splitting, or worse: diagnostic folly.

Diagnostic charting of the stretch between distress and depression has been chaotic and thus confusing. Pincus *et al.* (1999) point out that the term minor depression has been defined in nine different ways, the concept of subthreshold depression in five different ways; depressive symptoms, also called subthreshold depressive symptoms or depressive symptoms only, were defined in three different ways; mixed anxiety-depression disorder in four different ways. Two different symptom lists were used to define recurrent brief depression. The minimum number of symptoms required for a diagnosis of subthreshold mood disorder ranged from one to six. Duration has not been uniformly specified, and impairment criteria have not been standardized or are not mentioned at all.

The various subtypes of depression, moreover, show little stability; i.e. in many depressed patients diagnoses change over time, while the various subtypes often occur comorbidly (Angst *et al.*, 2000; Chen *et al.*, 2000).

The prevailing nosological classification system, meant to end all ambiguities in the diagnosis of depression, has thus set in motion a regressive movement putting us back in a chaotic situation reminiscent of that of yesteryear. The methodological concerns expressed shortly after the introduction of the DSM by Van Praag (1982a,b) are now shared by a number of investigators (Goldberg, 1996; Van Os *et al.*, 1996; Krueger *et al.*, 1998; Krueger, 1999; Vollebergh *et al.*, 2001). Judd *et al.* (1997), for instance, hypothesized a single disease hypothesis underlying the depressive spectrum and named it: unipolar depressive disease with pleiomorphic expressions. The question remains, can we and should we distinguish the various

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expression forms of that disease? Angst *et al.* (2000), recognizing the shortcomings of nosologically based systems, concluded that depression is better represented on a continuum, than as a category. The continuum, they propose, should be based on three dimensions, i.e. number of symptoms, duration and recurrence. Number of symptoms, however, is a crude criterion, subinformative if the nature of the symptoms is not specified.

As a consequence of the proliferation of new diagnostic constructs another problem is magnified, i.e. the comorbidity problem (Van Praag, 1996). The majority of psychiatric patients qualify for a series of (axis I and axis II) diagnoses, the group of mood disorders being a telling example. Various mood disorders often occur combined. Co-occurrence of mood disorders with anxiety disorders and with various personality disorders reaches values up to 60–80%. The greater the number of available categories, the greater the average number of diagnoses per patient will be. The comorbidity problem is thus greatly magnified and comorbidity is a true plague for psychiatric research, most particularly for biological research. By way of an example: one studies a patient with major depression and traces a biological disturbance or an effect of a particular medication. That same patient, however, qualifies for several other axis I and axis II diagnoses. What now is the behavioural correlate of the biological finding? Which of the various diagnoses responded to the medication? The depression, or one of the other diagnoses or components of those diagnoses? We do not know, and in most cases this issue is simply ignored. With avoidance behaviour, however, no problem can be properly resolved (Van Praag, 1989, 1993, 1998, 2000).

A final weakness of the nosological approach is that it forces us to draw borders; borders between discrete categories and borders between disorders and normality. The first exercise is fraught with difficulties because of substantial overlap between neighbouring entities. The latter problem is even more complicated. How can one draw the border between sadness and depression, between worrying and a pathological mood change, in a way that makes sense in terms of therapeutic measures to be taken, and in terms of predicting course and ultimate outcome of these conditions? Is it by counting the number of symptoms, by assessing their severity or duration, by measuring the degree of disability they cause, by estimating the measure in which mood state and preceding psychotraumatic experiences coincide, or in any other way? Answers are wanting; scientifically, this problem has been hardly touched. This dilemma, too, posits great problems for psychiatric research, again particularly for biological research. Suppose a test group is composed of both depressed patients and 'worriers'. The chance that one will be able to trace a biological determinant or concomitant of depression, or to provide a valid estimate of the therapeutic potential of a new antidepressant, will be considerably reduced. By way of an analogy: one would have had little chance of discovering the cause of

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tuberculosis if the experimental group had been composed of tuberculous patients and patients suffering from a common cold (see also Chapter 9).

In short, the nosological approach is in several major ways a diagnostic liability. True, it is handy in terms of communicability, but weak in characterizing adequately the mental disorders seen in actual practice. Convenience is obtained at the expense of diagnostic exactitude. One can even rightfully raise the question whether it will ever be possible to distinguish sorrow from depression, using discrete categories as units of classification to systematize mental pathology. So far biological research does not provide much hope. In a PET study by Mayberg *et al.* (1999), for instance, it was found that in normal sadness and depression the same changes in energy consumption occur and in the same brain regions.

1.2.3 The syndromal approach

Depressions can be diagnosed according to the prevailing syndrome. In this approach symptomatology is the only criterion used. Other relevant variables such as course, causational factors and treatment response are recorded on separate axes, independent of each other and independent of the syndrome.

This was the approach proposed by Van Praag and collaborators and used by them, from the late 1950s on, in their early biological and psychopharmacological studies of depression (Van Praag & Leijnse, 1962, 1963a,b). Three syndromes were distinguished, named vital depression, personal depression and the mixed syndromes. The symptom composition of the various syndromes was characterized as well as the impact severity has on their manifestation forms. Moreover, a standardized, structured interview was developed to assess and record those syndromes (Van Praag *et al.*, 1965).

The best fitting diagnostic analogue of vital depression in today's vocabulary, is the syndrome described under the heading of major depression, melancholic type, and that of personal depression the one subsumed under the heading dysthymia. Mixed depressions are made up of components of vital and personal depression.

The DSM system has abandoned precise syndromal differentiation. Symptomatically, x out of a series of y symptoms suffice for a particular diagnosis, regardless of which ones. The same diagnosis, thus, covers a variety of syndromes. This approach did not refine psychiatric diagnosing. In the domain of mood disorders, for one, there is sufficient evidence that syndromal distinctions make sense, at least therapeutically (Van Praag, 1962; Heiligenstein *et al.*, 1994; Roth, 2001).

Independent scoring of the prevailing syndrome and the various non-symptomatological criteria was deemed necessary, since no clear mutual relationships had been established. Not until such relationships have been made plausible can one speak of a disease entity; or better: an entity in gestation. A true entity requires that its pathophysiology has been elucidated.

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For most diagnostic constructs recognized today, mutual relationships, as referred to above, have still to be established. Yet the DSM system takes them for granted and hence the validity of the system is questionable.

1.2.4 Problems inherent to the syndromal approach

The syndromal approach to (depression) classification is also burdened with problems.

First of all, syndromes frequently appear in incomplete form or jointly with other (complete or incomplete) syndromes. This prompts clinicians and researchers alike to expand the stock of syndromes ever more. An example is the following. Quite often patients are seen with depressions showing all the symptoms of the vital depressive syndrome (in short: vital depression) save diurnal fluctuation of symptoms and in whom mood lowering is reactive, meaning that the capacity to be cheered up by positive events remains intact. We have distinguished this syndrome as 'pseudo' vital depression, from 'true' vital depression, a syndrome that fluctuates diurnally in severity and in which mood lowering is stable even if positive events happen. We realized soon that there exist many more such distinctions, and that consequently, such splitting is truly a process without an end, and thus probably fruitless.

Secondly, the severity of a syndrome is usually expressed as a sum score on a symptom rating scale. Inter-individually, and over time intra-individually, the severity of each individual symptom may vary considerably. Symptoms like anxiety, anhedonia and motor retardation as they appear in vital depression, range from being prominent to a position of minor importance. Those differences are blurred by the instruments syndromes are generally assessed with.

1.2.5 The dimensional/functional approach

A third diagnostic method is the one in which the abnormal mental state is dissected in its component parts, the psychopathological symptoms, whereupon each component is assessed as to its severity. This approach can be called dimensional.

Psychopathological symptoms, however, are actually effigies. They are the expression forms of underlying psychic dysfunctions. Psychopathological symptoms are the way those dysfunctions are experienced by the patient and observed by the investigator. Hearing voices for instance is a symptom, a particular perceptual disturbance the underlying dysfunction. Anhedonia is a symptom, the inability to couple a particular perception to the corresponding emotion the underlying dysfunction.

Symptom analysis of an abnormal mental state, therefore, should be followed by attempts to elucidate, assess and preferably measure the underlying psychic dysfunctions. This was the method Van Praag proposed when syndromal classification

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proved to be difficult to handle in clinical practice and research (Van Praag & Leijnse, 1965; Van Praag, 1997, 2001) The name *functional psychopathology* was coined for this approach. The advantages it yields are considerable.

Psychic dysfunctions are measurable, many of them even quantitatively; this in contrast to syndromes and disease entities. Via the functional approach psychiatric diagnosing will, at last, be elevated to a true scientific level. Moreover, this method provides the diagnostician with a map of the 'psychic apparatus', indicating which of its components function within normal limits and which of them are disrupted. This is of great importance for clinicians: it provides them with focal points to direct treatment at; biological as well as psychological treatment. It is equally important for the researcher, particularly the biological researcher, because it provides a precise delineation of the behavioural aberrations, the biological underpinnings of which one aims to elucidate.

The methods to implement functional analysis of psychopathological states do not yet lie ready. Partly they have still to be developed, partly they have to be refined. In order to accomplish this task intensive collaboration of research psychiatrists and experimental clinical psychologists is needed.

The shortcomings of the dimensional/functional method are of a practical nature. Diagnoses cannot be condensed any more into a single construct, such as major depression or dysthymia. It requires a mouthful of scores and this will hamper professional communication.

1.3 Multi-tier diagnosing

The various diagnostic strategies are by no means mutually exclusive but rather complementary. They should be combined in a comprehensive diagnostic approach consisting of the following steps.

- 1 Characterization of the nosological cluster the mental disorder belongs to.
- 2 Precise syndrome analysis.
- 3 Symptom analysis of the syndrome or (part of) syndromes the disorder consists of.
- 4 Analysis of the psychic dysfunctions underlying the psychopathological symptoms. This effort still lies largely in the experimental realm.
- 5 Assessment of the severity, duration, course of the syndrome and of premorbid personality features, *independent* of the syndrome and *independent* of each other.
- 6 The disabilities the disorder has inflicted will be charted.

This comprehensive approach is not being used in present-day psychiatry, neither in practice nor in research. The nosological approach governs and controls psychiatric diagnosing. Whatever the aim is of the research programme: the biology of depression, its response to psychotropic drugs or psychological interventions,

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its epidemiology or any other issue, starting point and endpoint are the discrete categories distinguished by the DSM system, or any of the new constructs not yet DSM-sanctioned. Psychiatric diagnosing is locked up in a nosological straitjacket, and thus immobilized. Syndromal precision is a thing of the past. Symptom analysis remains in abeyance. Functionalization of psychiatric diagnosis as we have advocated for many years (Van Praag & Leijnse, 1965; Van Praag *et al.*, 1987; Van Praag, 2001) is not an idea that has so far sufficiently caught on and has not received large-scale investigational attention. The shortcomings of the nosological approach are disregarded, and diagnostic business continues to be carried out as usual.

This situation is harmful for psychiatric research, and life event research is particularly sensitive. Adversity leads inevitably to mood lowering. Mood disturbances seldomly appear alone but are generally accompanied by disturbances in other psychic domains resulting for instance in anxiety, irritability, loss of appetite, sleep disturbances or diminished susceptibility for pleasurable stimuli. Those appear in various combinations and different degrees of prominence.

Consequently, the border between distress and depression is blurred, not yet established and possibly impossible to ascertain. The study of the psychological impact of life events in an all or none fashion – i.e. investigating whether case-depression does or does not appear after adversity – is a limited approach, too distanced from real-life situations. Life event research, per excellence requires dimensional/functional analysis of stress-related psychopathology whereby the type of stress phenomena, their duration and intensity, their disruptive effects on professional, family and social life, and possible predisposing personality traits are each carefully studied, assessed and recorded. These issues seem to be at least as relevant as the question whether life events have or have not contributed to the aetiology of case-depression.

Yet, life event/stress research is not (yet) carried out in this manner. Hence, most data reviewed and discussed in this monograph, from sheer necessity, have reference to the construct of depression, as defined by the DSM, with the additional restriction that most studies pertain to major depression.

1.4 Conclusions

Several methods have been employed to diagnose mental pathology, in this case depression.

The nosological approach characterizes disorders conceived as discrete and separable entities. A certain resemblance notwithstanding, most of the entities so distinguished are utterly heterogeneous and seem to consist of a variety of conditions different with regard to symptomatology, course, outcome and treatment response. A nosological diagnosis, thus, provides no more than a crude impression of the character of the mental disorder one is dealing with.

The syndromal approach characterizes the phenomenology of the disorder and recognizes a number of discrete symptom clusters. This approach, too, runs frequently up against obstinate clinical realities. Syndromes rarely appear alone and in complete form, appearing much more frequently incomplete and jointly with other (incomplete) syndromes. Syndromal diagnoses, like their nosological counterparts, fail to define individual psychiatric patients in any detailed fashion.

The dimensional-functional approach dissects the syndrome(s) the patient presents, in its component parts, i.e. the psychopathological symptoms. Those symptoms are considered to be the expression forms of underlying disturbances in psychic regulatory systems. Attempts are being made to characterize, measure and record those dysfunctioning psychic domains. The dimensional-functional approach provides a detailed, precise and truly scientific depiction of an abnormal mental state. This approach find itself still largely in the experimental realm.

All three methods should be utilized to reach a precise understanding of the psychopathological structure of abnormal mental conditions. Unfortunately this is not the direction modern psychiatry has taken. Generally a diagnosis consists of just a nosological construct. Following this trend, most attention in stress research and life event research is focused on the question as to whether case-depression can be a stress product. The psychopathological consequences of life events and stress, however, can be very diverse, and to analyse those in detail the dimensional-functional approach is indispensable. So far, researchers in this field, however, do not walk in this way and therefore we have only a limited view on the psychological damage life events and resultant stress may inflict.

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