Limitations of the symptom-oriented approach to psychiatric research

RAMIN MOJTABAI and RONALD O. RIEDER

Background We critically reviewed the arguments of the symptom-oriented researchers who propose to replace syndromes and diagnostic categories with symptoms as units of analysis in psychiatric research.

Method Three central arguments were examined: (a) current diagnostic categories lack reliability and validity; (b) using diagnostic categories leads to misclassification and confounding; and (c) symptom-oriented theories are clearer, easier to test, and more likely to lead to an explanation of psychopathology. These arguments are based on three assumptions respectively: (a) symptoms have higher reliability and validity; (b) underlying pathological processes are symptom-specific; and (c) elucidation of the process of symptom development will lead to (and must precede) the discovery of the causes of syndromes.

Results We found little evidence supporting these assumptions and arguments based on them.

Conclusion There are no clear advantages in replacing syndromes with symptoms as units of analysis for psychiatric research.

Traditionally, 'syndromes' or diagnostic categories have been the units of analysis for research and practice in psychiatry. However, in recent years a number of investigators have proposed to replace syndromes with individual symptoms as units of analysis (Persons, 1986; Bentall, 1990; Costello, 1992). In support of their position, these authors refer to some limitations of the syndrome-oriented approach in comparison to the symptom-oriented approach, including: (a) the lack of adequate reliability and validity of diagnostic categories; (b) the problem of misclassification of cases and confounding of effects which arises in syndrome-oriented research; and (c) the difficulty of developing clear and testable hypotheses using diagnostic categories. We critically review these arguments and the assumptions underlying them.

In this paper we confine our discussion to schizophrenia as a syndrome or diagnostic category and delusions, hallucinations and to a lesser extent thought disorder, as symptoms. However, the arguments and conclusions can be generalised to other diagnostic categories and symptoms as well.

RELIABILITY AND VALIDITY OF DIAGNOSTIC CATEGORIES *V.* SYMPTOMS

Reliability

Argument

Reviewing the available interrater reliability studies of the diagnosis of schizophrenia, Costello (1993) concluded that these studies provide "no clear evidence for the reliability of the current and lifetime diagnoses of schizophrenic or schizophreniform disorders." Similarly, Bentall (1992) commented that:

> "Various different sources of disagreement about the diagnosis of schizophrenia have become apparent from research. For example, early studies not only showed that there was poor agreement between clinicians about who merited the diagnosis . . . but that there were also important differences between the diagnostic practices of psychiatrists in different countries."

Assumption

The criticism of low reliability of diagnostic categories is based on an implicit comparison with the reliability of symptoms; a comparison made explicit by Costello (1993) when he wrote: "agreement could be reached more quickly on the measurement of symptoms than on the inclusion and exclusion criteria for diagnoses."

Evidence

The evidence from interrater reliability studies of diagnoses and symptoms, at least in the case of schizophrenia, do not prove symptoms to be more reliable than the diagnosis (Table 1). The mean reliability for the diagnosis of schizophrenia in the three studies reviewed in Table 1 was 0.8 (unweighted mean), whereas the mean reliability for the individual or groups of symptoms was only 0.5. In every one of the three studies, the mean reliability of symptoms was lower than for the corresponding diagnosis (Table 1). Although the reliability of a symptom or a diagnosis depends on a combination or rater, instrument and contextual factors, it is fair to assume that in studies assessing the reliability of diagnoses and symptoms simultaneously, these factors would affect the assessments of both to a similar degree.

Comparing the reliability of syndromes with the reliability of their constituent symptoms is analogous to the comparison of the reliabilities of tests and their constituent items (Blashfield & Livesley, 1991). As predicted by psychometric theory, the reliability of a test is generally higher than the individual items. Similarly, the reliability of the diagnosis can be expected to be at least as high as the reliability of its constituent symptoms.

Validity

Argument

Bentall (1992) and Costello (1992) have criticised the syndromes that comprise the current diagnostic categories for lack of validity. This argument is often based on the lack of adequate agreement between different diagnostic systems in representing the same diagnostic category, or in other words lack of concurrent validity. As Costello (1992) wrote:

Table I Interrater reliability estimates for the diagnoses and the symptoms of schizophrenia from three studies using structured interviews (adopted from Andreasen *et al*, 1982; Endicott *et al*, 1982; Andreasen *et al*, 1992)

	Andreasen *et al*, 1982[1]	Endicott *et al*, 1982[2]	Andreasen *et al*, 1992[3]
Diagnosis of schizophrenia	1.0	0.80	0.61–0.86[4]
Symptom categories			
Delusions	0.88	0.34[5]	0.64
Hallucinations	0.65	0.39[5]	0.76
Bizarre (disorganised) behaviour	0.82	0.73	0.30
Positive thought disorder	0.56[5]	–	0.00
Inappropriate affect	0.62	–	0.67
Affective flattening	0.70	0.13	0.71
Alogia	0.14	–	0.45
Anhedonia	–	–	0.60
Avolition	–	–	0.53
Attention	–	–	0.27
Mean reliability of symptom categories	0.62	0.40	0.49

1. Interrater reliability was based on information about symptoms occurring during the current episode or the past year. Kappa was calculated for diagnosis and intraclass correlation for symptoms.
2. Interrater reliability of diagnosis and symptoms was based on both current and historical information. Kappa was calculated for both diagnosis and symptoms. The kappa for diagnosis according to DSM–III (American Psychiatric Association, 1980) criteria is reported here.
3. Interrater reliability was based on information about the presence of symptoms "much of the time since onset". Kappa was calculated for diagnosis and intraclass correlation for the global rating of the symptoms.
4. The kappa for a diagnosis of schizophrenia was 0.61 and for a diagnosis of schizophrenia spectrum 0.86.
5. The values represent mean ratings for variable numbers of specific symptoms (e.g. different forms of delusion or hallucination) under each general symptom category.

> "When a number of procedures, supposedly measuring the same phenomenon, have poor concurrent validity, their construct validity becomes suspect. Consequently, the meaning of any data relating to differences between diagnostic groups or relating to the correlates of any diagnosis is unclear."

With regard to stability of syndromes, Bentall (1990) commented that:

> "on re-examination with the same criteria after several years many patients are assigned to a different diagnosis than the one they originally received."

Assumption

Presenting the lack of agreement between different diagnostic systems or lack of stability as arguments for choosing the symptom approach is based on the assumption that there is less disagreement between the different definitions of symptoms or the clinicians' understanding of these definitions, and that symptoms have more stability.

Evidence

Although the evidence for concurrent validity of diagnostic systems is not encouraging, there is some evidence that, at least in the case of schizophrenia, this is partly due to over-reliance on symptoms measured cross-sectionally. Systems that use early course of illness in defining the diagnosis show higher agreement. For instance Helzer *et al* (1981) observed that the concordance between the Feighner criteria of schizophrenia (Feighner *et al*, 1972) and DSM–III (American Psychiatric Association, 1980) criteria, both of which include a minimum of six months' duration, is larger than that between systems which are solely based on cross-sectional symptomatology (kappa of 0.84 between Feighner and DSM–III *v.* 0.44–0.67 between three cross-sectional systems).

In addition, there is considerable disagreement between different definitions of symptoms and also the different raters' understanding of these definitions. For instance, in their classic study using the Present State Examination (PSE; Wing *et al*, 1974), Strauss *et al* (1969) observed that among their series of 119 patients with schizophrenia:

> "there were as about one-half as many questionable delusions as there were definite delusions . . . almost three-quarter as many questionable hallucinations as definite hallucinations . . . raters develop conventions regarding how strict they will be in accepting responses as positive proof of presence or absence of these phenomena."

Costello (1993) himself admits that "symptoms are quite complex and therefore their assessment is not likely to be a straightforward and noncontroversial matter."

With regard to the stability of diagnoses using the same criteria, at least in the case of schizophrenia, there is strong evidence. For instance, in their 30- to 40-year follow-up study, Winokur & Tsuang (1996) reported a high stability between diagnosis of schizophrenia at index hospitalisation and diagnoses at short-term and long-term follow-ups. Based on this finding they concluded that:

> "Regardless of the specific method used, it is clear that schizophrenia is quite stable. Ninety-three to 95% of the patients continued to have the diagnosis of schizophrenia."

On the other hand, as Persons (1986) noted, symptoms:

> ". . . are more transient than diagnostic labels. Symptoms of thought disorder may be present at one moment or in one context, but absent at a later moment or in a different context."

Other indicators of validity

The validation of diagnostic categories should not be limited to evaluation of agreement between different systems or stability of diagnoses. Longitudinal studies, family aggregation studies and search for laboratory markers are the other means for validating a diagnostic category (Robins & Guze, 1970). Much evidence from longitudinal studies support the predictive validity of a schizophrenia diagnosis for course and outcome of illness (Winokur & Tsuang, 1996). Evidence from family aggregation and twin studies also support the validity of schizophrenia (Gottesman, 1991; Torrey *et al*, 1994).

Just as syndromes are constructs in need of validation, so are symptoms. It is a legitimate question to ask whether specific symptoms predict the course of a disorder, response to treatment or biological correlates. As an example, Crichton (1996) has argued for discarding the First Rank Schneiderian symptoms because of the lack of evidence for such validity. The predictive validity of other symptoms of schizophrenia have not been much better. For instance, Carpenter *et al* (1978) found no association between the positive symptoms of schizophrenia (which include delusions and hallucinations) and the five-year course of the illness. Also, in their review of

literature, Pope & Lipinski (1978) concluded that there is little evidence that positive symptoms of schizophrenia are of prognostic significance.

Evidence for the heritability of specific symptoms in twin studies (Slater, 1971; Berenbaum *et al*, 1987) as well as sibling studies (Kendler *et al*, 1997; Hwu *et al*, 1997) have been similarly discouraging. For instance, in Kendler *et al*'s (1997) study of the resemblance of symptoms over the entire course of illness in sibling pairs concordant for schizophrenia, the Spearman rank correlation for seven psychotic symptoms ranged between 0.05 and 0.23 (median=0.15). Similarly, Hwu *et al* (1997) reported a kappa of 0.30 for concordance in sibling pairs of delusions and hallucinations, 0.30 for thought disorganisation and 0.35 for negative symptoms. Berenbaum *et al*'s (1987) conclusion from their study represents a fair summary of the findings of the studies of heritability of symptoms in general:

> "None of the symptoms we examined, positive or negative appeared to be nearly as heritable as the global diagnosis of schizophrenia. This result is consistent with the hypothesis that schizophrenics inherit a common underlying factor that predisposes them to develop any of several overt symptoms . . ."

Laboratory studies of schizophrenia and most other psychiatric disorders have provided little in the way of validation of syndromes or symptoms. However, the available data suggest that the syndrome of psychosis, rather than the individual symptom, is the proper unit of analysis. The misuse of drugs with dopaminergic activity (i.e. cocaine and amphetamines) produce psychotic syndromes and not isolated symptoms (Fibiger, 1991), and neuroleptics usually lead to a global improvement in all psychotic symptoms (Johnstone, 1978).

MISCLASSIFICATION AND CONFOUNDING

Argument

Both Persons (1986) and Costello (1992) have argued that using syndromes as the units of analysis in studying the underlying processes of symptoms leads to misclassification. An example from Costello (1993) illustrates this argument. Imagine that a researcher who wants to study the underlying processes of thought disorder compares patients with schizophrenia to patients with other mental illnesses. This research strategy, Costello argues, will lead to misclassification of cases because:

> "(a) not all schizophrenics have thought disorder . . . (b) schizophrenics who are thought-disordered are only episodically so, and their thinking may not be disordered during the testing session; (c) patients with non-schizophrenic diagnoses, such as bipolar depression, may have symptoms of thought disorder." (Costello, 1993)

The proper subjects for the study of the processes involved in thought disorder, he argues, should be patients with thought disorder. In such a study, it is implied, diagnostic category would be irrelevant.

In addition, Persons (1986) and Costello (1992) have argued that grouping according to diagnostic category may lead to confounded results. In a study of thought disorder which compares patients with schizophrenia with patients having other diagnoses, any difference between the two groups of patients could be a result of thought disorder, schizophrenia or an interaction of these two. Perhaps based on such reasoning, many symptom-oriented researchers completely ignore diagnosis in their work (Bentall & Slade, 1985).

Assumption

Implicit in this argument is the assumption that the underlying processes of psychopathology are symptom-specific and not syndrome-specific. In other words, similar symptoms are caused by the same pathological processes across different diagnostic categories. For instance, thought disorders in schizophrenia and bipolar disorder result from the same underlying processes. This view, which in one form or other is a fundamental tenet of the symptom approach, was expressed most forcefully by van Praag (1997):

> "The search for markers and eventually causes of discrete mental disorders would be largely futile . . . Not schizophrenia, panic disorder or major depression, as such, will be studied, but disturbances in perception, in information processing, in mood regulation . . . A biology of psychological dysfunctions as they occur in dysfunctional mental states would thus be the ultimate goal of biological psychiatric research."

Bentall (1990) envisioned a classification of symptoms which is based on the specific underlying processes for each symptom across diagnoses:

> ". . . it should be possible to identify which kinds of cognitive abnormalities are implicated in which symptoms, and to thereby construct a 'cognitive table' of psychopathological state analogous to the periodic table in chemistry."

However, the assumption of symptom-specificity of underlying processes remains largely unexamined and researchers who, based on this assumption, ignore diagnostic categories are themselves at risk for confounding.

Confounding in the symptom approach

Admittedly, in a study of the underlying processes of a specific symptom, subjects should be selected on the basis of the presence or absence of that symptom. If the subjects are selected on the basis of diagnosis alone, the findings can be attributed to the symptom, the diagnosis or an interaction of the two. But, what would happen if patients with the symptom, irrespective of diagnosis, are selected into the target group and patients without the symptom, again irrespective of diagnosis, into the control group? Could the findings from this study be attributed purely to the symptom? The answer would be positive only when one of the following two conditions are met: (a) we can assume that diagnosis has no impact on the underlying processes and these processes are completely symptom-specific; or (b) the proportion of patients from the different diagnostic groups in the target and control groups are similar. The first condition, as we noted earlier, remains an unexamined assumption. The second condition requires the base rates of the symptom in the different diagnostic groups to be equal – a condition that rarely holds. When the base rates for the symptom are not equal, ignoring diagnosis can, paradoxically, lead to confounding.

An example helps to illustrate this point. Winokur & Tsuang (1996) reported that 54% of their patients with schizophrenia and 15% of their patients with mania reported auditory hallucinations. Assuming equal prevalence of schizophrenia and mania, the researcher who selects patients with auditory hallucinations irrespective of their diagnosis from a mixed group of patients with equal numbers having schizophrenia and mania will end up with a group of hallucinating patients of whom about 80% have a diagnosis of schizophrenia and 20% mania; and a non-hallucinating comparison group of which about 35% have schizophrenia and 65% mania. Now, any difference between the two groups can be attributed to auditory hallucinations, diagnosis or the interaction

of these two. In other words findings will be confounded by diagnosis.

An actual example of potential confounding in symptom approach research is the study by Huq *et al* (1988), in which patients with delusion showed abnormalities in probabilistic reasoning. All the delusional patients had a diagnosis of schizophrenia; whereas none in the comparison group had such a diagnosis. Therefore, the findings can be attributed to delusions, schizophrenia, or an interaction of the two.

NATURE OF THEORIES IN SYMPTOM APPROACH

Argument

Persons (1986) has argued that "the symptom approach makes it easier to formulate hypotheses about underlying mechanisms" and "allows for tighter, more elaborated explanatory links between proposed underlying mechanisms and the overt phenomena . . .". On the other hand, diagnostic categories "make it surprisingly difficult for the researcher to be clear about the hypothesis his or her study was to test." The theoretical appeal of the hypotheses formulated in the symptom approach is stressed in one way or another by other proponents of this approach as well. For example, Costello (1992) has argued that symptom approach is more conducive to the study of the dimensional–categorical issue of psychiatric phenomena and to the development of animal models of psychopathology.

Assumption

In suggesting the replacement of syndrome approach hypotheses with those from symptom approach, it is assumed that the two sets of theories 'explain' the same constructs, and that elucidation of the underlying processes of symptom development will lead to an explanation of the causes of mental disorder. Even when the distinction between the constructs addressed by different theories is recognised, it is often assumed (and sometimes stated) that the explanation of symptoms must necessarily precede that of syndromes:

> "Abnormalities of cognitive organization (the final common pathway of symptoms) may, in turn, be a consequence of a wide range of biological (genetic, biochemical, neurological) and historical (environmental) factors, but this second level of explanation will necessarily come later (biochemical abnormalities alone, for example, cannot *explain* mental disorder unless it can also be shown how they affect cognitive organization)." (Bentall, 1990)

Evidence

Symptom approach theories (e.g. Huq *et al*, 1988; Frith & Done, 1988; Bentall *et al*, 1994) generally attempt to explain the pathopsychology of psychiatric symptoms, analogous to the pathophysiological theories of physical symptoms. Van Praag (1997) described this process in his discussion of the 'functionalisation' of syndromes, that is, dissecting syndromes into the psychological dysfunctions which underlie symptoms:

> " 'Functionalisation' of psychiatric diagnoses, systematically carried out, will ultimately lead to the equivalent of what patho-physiology is for somatic medicine: the discipline providing an understanding of what the deflections in the psychological apparatus are that underlie a particular psychiatric disorder." (van Praag, 1997)

If an investigator focuses only on one or two symptoms, it does allow for 'tighter' and 'more elaborated' theories to be posited, if by 'tighter' one means more directly and immediately connected with the symptom. Bentall *et al*'s (1994) theory of attributional bias for persecutory delusions is an example of such a theory which attempts to make a symptom understandable. However, these theories do not explain the aetiology of the disorder. They do not tell us what predisposed one person and not another to develop schizophrenia, or what triggered the disturbance in the predisposed individual. Such aetiological hypotheses are often proposed and studied for syndromes. The genetic and the diathesis/stress models of schizophrenia are examples of such aetiological theories. Even though both the pathopsychological and aetiological theories claim to explain the 'underlying mechanisms' of illness, usually they do not directly contradict each other and can coexist because they link psychopathology to different realms.

Is understanding of pathopsychology necessary for the discovery of aetiology?

A review of the history of the aetiological discoveries in medicine or psychiatry does not support the argument that explanation of symptoms must precede that of syndromes. For instance, understanding the pathological processes in thermo-regulation which underlie the symptom of fever was not necessary for the discovery of the causes of infectious diseases. Similarly, understanding the psychopathology of symptom production was not necessary for discovering the causes of three classic neuropsychiatric disorders, of general paralysis of the insane, pellagra, and the Wernicke–Korsakoff psychosis. It was rather the careful delineation of these once common psychiatric syndromes and the study of their correlates (e.g. historical information, association with nutritional patterns) that led to the discovery of their causes and effective interventions.

THE PLACE OF SYMPTOM APPROACH

As we argued in previous pages, syndrome approach and symptom approach research often have different aims and answer different questions. Where the question is the aetiology of mental disorders, syndromes appear to be the most suitable units of analysis. Where the question is the pathopsychological or pathophysiological mechanisms of a symptom or a cluster of symptoms, then the symptoms themselves appear to be the most suitable units of analysis. However, clearer description and delineation of syndromes is dependent on clearer descriptions and delineation of symptoms. Here, research on symptoms has much to contribute to syndrome approach research. The improvement in reliability and even validity of diagnoses based on modern structured interview instruments is an evidence of the importance of attention to symptoms in syndrome research. In addition, symptom approach research has much to contribute in designing symptom-focused treatments and in understanding the subjective experiences of patients.

It is possible, even likely, that the current diagnostic categories such as schizophrenia do not represent specific aetiological entities, as the evidence of heterogeneity (Andreasen *et al*, 1995) and lack of concordance between different validators (Kendler, 1990) suggest. However, for the purpose of research or practice, it is feasible to define more specific, and perhaps more homogeneous, sub-syndromes on the basis of clustering of symptoms or individual validators (e.g. negative symptom schizophrenia, neuroleptic-resistant schizophrenia, familial manic–depressive psychosis; Rieder, 1974). This

may allow an integration of the symptom and syndrome approaches. It may even be more valuable to define sub-syndromes based on pathophysiological traits or 'endophenotypes' (Gottesman, 1991), that is, indicators which are not available to the naked eye and are intermediate to the phenotype and genotype. Groups based on such indicators may be more useful for elaboration of aetiological mechanisms than symptoms would be.

We predict that any symptom approach researchers who attempt to go beyond the confines of individual symptoms to explain the associations between symptoms (Andreasen *et al*, 1995) or the similarity in their response to treatment (Johnstone, 1978), would rediscover syndromes resembling the traditional syndromes. We are not alone in this speculation. Spitzer (1975), in his response to Rosenhan's (1973) criticism of psychiatric diagnosis, predicted such a rediscovery of syndromes in an imaginary future where the symptom approach dominates:

> "I have a vision. Traditional psychiatric diagnosis has long been forgotten. At a conference on behavioural classification, a keen research investigator proposes that the category 'hallucinations of unknown etiology' be subdivided into three different groups based on associated symptomatology. The first group is characterized by depressed affect, diurnal mood variation, and so on, the second group by euphoric mood, psychomotor excitement . . ." (Spitzer, 1975)

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REFERENCES

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (DSM–III) (3rd edn). Washington, DC: APA.

Andreasen, N. C., McDonald-Scott, P., Grove, W. M., *et al* (1982) Assessment of reliability in multicenter collaborative research with a videotape approach. *Approach Journal of Psychiatry*, **139**, 876–882.

—, Flaum, M. & Arndt, S. (1992) The comprehensive assessment of symptoms and history (CASH): An instrument for assessing diagnosis and psychopathology. *Archives of General Psychiatry*, **49**, 615–623.

—, Arndt, S., Alliger, R., *et al* (1995) Symptoms of schizophrenia. *Archives of General Psychiatry*, **52**, 341–351.

Bentall, R. P. (1990) The syndromes and symptoms of psychosis: Or why you can't play twenty questions' with the concept of schizophrenia and hope to win. In *Reconstructing Schizophrenia* (ed. R. P. Bentall), pp. 23–60. London: Routledge.

— (1992) The classification of schizophrenia. In *Schizophrenia: An Overview and Practical Handbook* (ed. D. J. Kavanagh), pp. 23–44. London: Chapman and Hall.

— & Slade, P. D. (1985) Reality testing and auditory hallucinations: A signal detection analysis. *British Journal of Clinical Psychology*, **24**, 159–169.

—, Kinderman, P. & Kaney, S. (1994) The self, attributional processes and abnormal beliefs: Towards a model of persecutory delusions. *Behavioural Research and Therapy*, **32**, 331–341.

Berenbaum, H., Oltmanns, T. F. & Gottesman, I. I. (1987) A twin study perspective on positive and negative symptoms of schizophrenia. In *Positive and Negative Symptoms of Psychosis* (eds P. D. Harvey & E. F. Walker), pp. 50–67. Hillside, NJ: Lawrence Erlbaum.

Blashfield, R. K. & Livesley, W. J. (1991) Metaphorical analysis of psychiatric classification as a psychological test. *Journal of Abnormal Psychology*, **100**, 262–270.

Carpenter, W. T., Bartko, J. J., Strauss, J. S., *et al* (1978) Signs and symptoms as predictors of outcome: A report from the International Pilot Study of Schizophrenia. *American Journal of Psychiatry*, **135**, 940–944.

Costello, C. G. (1992) Research on symptoms versus research on syndromes: Arguments in favour of allocating more research time to the study of symptoms. *British Journal of Psychiatry*, **160**, 304–308.

— (1993) Advantages of the symptom approach to schizophrenia. In *Symptoms of Schizophrenia* (ed. C. G. Costello), pp. 1–26. New York: Wiley.

Crichton, P. (1996) First-rank symptoms or rank-and-file symptoms? *British Journal of Psychiatry*, **169**, 537–540.

Endicott, J., Nee, J., Fleiss, J., *et al* (1982) Diagnostic criteria for schizophrenia. *Archives of General Psychiatry*, **39**, 884–889.

Feighner, J. P., Robins, E. & Guze, S. B. (1972) Diagnostic criteria for use in psychiatric research. *Archives of General Psychiatry*, **26**, 57–63.

Fibiger, H. C. (1991) The dopamine hypotheses of schizophrenia and mood disorders: Contradictions and speculations. In *The Mesolimbic Dopamine System: From Motivation to Action* (eds P. Willner & J. Scheel-Krüger), pp. 615–637. New York: Wiley.

Frith, C. D. & Done, J. (1988) Towards a neuropsychology of schizophrenia. *British Journal of Psychiatry*, **153**, 437–443.

Gottesman, I. I. (1991) *Schizophrenia Genesis*. New York: W. H. Freeman.

Helzer, J. E., Brockingham, I. F. & Kendell, R. E. (1981) Predictive validity of DSM–III and Feighner definitions of schizophrenia: A comparison with Research Diagnostic Criteria and CATEGO. *Archives of General Psychiatry*, **38**, 791–797.

Huq, S. F., Garety, P. A. & Hemsley, D. R. (1988) Probabilistic judgements in deluded and non-deluded subjects. *Quarterly Journal of Experimental Psychology*, **40**, 801–812.

Hwu, H. G., Wu, Y. C., Lee, S. F. C., *et al* (1997) Concordance of positive and negative symptoms in coaffected sib-pairs with schizophrenia. *American Journal of Medical Genetics*, **74**, 1–6.

Johnstone, E. C., Crow, T. J., Frith, C. D., *et al* (1978) Mechanism of the antipsychotic effect in the treatment of acute schizophrenia. *Lancet*, *i*, 848–851.

Kendler, K. S. (1990) Towards a scientific psychiatric nosology: Strengths and limitations. *Archives of General Psychiatry*, **47**, 969–973.

—, Karkowski-Shuman, L., O'Neill, F. A., *et al* (1997) Resemblance of psychotic symptoms and syndromes in affected sibling pairs from the Irish study of high-density schizophrenia families: Evidence for possible etiologic heterogeneity. *American Journal of Psychiatry*, **154**, 191–198.

Persons, J. B. (1986) The advantages of studying psychological phenomena rather than psychiatric diagnoses. *American Psychologist*, **41**, 1252–1260.

Pope, H. G. & Lipinski, J. F. (1978) Diagnosis in schizophrenia and manic–depressive illness. *Archives of General Psychiatry*, **35**, 811–828.

Rieder, R. O. (1974) The origins of our confusion about schizophrenia. *Psychiatry*, **37**, 197–208.

Robins, E. & Guze, S. B. (1970) Establishment of diagnostic validity in psychiatric illness: Its application to schizophrenia. *American Journal of Psychiatry*, **126**, 107–111.

Rosenhan, D. L. (1973) On being sane in insane places. *Science*, **179**, 250–258.

Slater, E. (1971) Psychotic and neurotic illnesses in twins. In *Man, Mind and Heredity: Selected papers of Eliot Slater on Psychiatry and Genetics* (eds J. Shields & I. I. Gottesman), pp. 88–130. Baltimore, MD: Johns Hopkins Press.

Spitzer, R. L. (1975) On pseudoscience in science, logic in remission, and psychiatric diagnosis: A critique of Rosenhan's "on being sane in insane places." *Journal of Abnormal Psychology*, **84**, 442–452.

Strauss, J. S. (1969) Hallucinations and delusions as points on continua function: Rating scale evidence. *Archives of General Psychiatry*, **21**, 581–586.

Torrey, E. F., Bowler, A. E., Taylor, E. H., *et al* (1994) *Schizophrenia and Manic-Depressive Disorder*. New York: Basic Books.

Van Praag, H. M. (1997) Over the mainstream: Diagnostic requirements for biological psychiatric research. *Psychiatry Research*, **72**, 201–212.

Wing, J. K., Cooper, J. E. & Sartorius, N. (1974) *The Measurement and Classification of Psychiatric Symptoms*. London: Cambridge University Press.

Winokur, G. & Tsuang, M. T. (1996) *The Natural History of Mania, Depression and Schizophrenia*. Washington, DC: American Psychiatric Press.

RAMIN MOJTABAI, MD, RONALD O. RIEDER, MD, Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, USA

Correspondence: Dr R. Mojtabai, 200 Haven Avenue, Apt. #6P, New York, NY 10033, USA

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