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Baseline Neuroendocrine Function and Diagnostic Stability Among Patients with a Nonmanic Psychosis

William Coryell, Mark Zimmermann, Georg Winokur, and Remi Cadoret

The University of Iowa, Department of Psychiatry, 500 Newton Road, Iowa City, IA 52242, USA

Summary. Psychotic patients underwent a dexamethasone suppression test (DST), careful diagnostic assessments at baseline and diagnostic reevaluations after 1 year. The predicted associations between baseline DST results and diagnosis were much clearer after prospective observation.

Key words: Schizophrenia – Neuroendocrine – Diagnosis

Introduction

The separation of psychotic depression from schizophrenia is among the most important in psychiatry; the appropriate treatments differ markedly as do the prospects for complete recovery, with or without contemporary treatments. Moreover, replicable psychiatric research depends on diagnostic homogeneity; obviously investigators who describe the phenomenological, genetic or biological features of schizophrenia assume that the large majority of the schizophrenics they study will not eventually prove to have other illnesses.

Clinicians often delay firm diagnostic assignments pending a period of inpatient observation or close outpatient follow-up, particularly when the patient presents atypical features or is a poor informant. Such patients are common among those presenting with functional psychoses and, indeed, many of these diagnostic ambiguities resolve with weeks or months of follow-up (Croughan et al. 1979; Liss et al. 1972).

Typically, though, psychotic conditions force treatment soon after admission. Moreover, research efforts rarely afford inclusion criteria based on prospective observation. Thus, any cross-sectional measure shown to reliably reduce diagnostic uncertainty could serve an important function, both in research and clinical practice.

The dexamethasone suppression test (DST) has shown promise as such a factor. A review of relevant studies (Coryell 1984) included five in which the test had 100% specificity to depression versus schizophrenia with a pooled sensitivity of 135/282 or 48%. Though DST results appeared much less specific towards affective disorder in many of the other studies reviewed, the field has never reconciled these with the clearly positive ones.

Discordant studies may well have differed by overall diagnostic certainty. Patients in one study may, because of referral patterns or catchment area peculiarities, have presented more difficult diagnostic problems; clinicians in other studies may have under-utilized previous medical records or outside informants, and clinicians in still other studies may have been relatively casual in applying research criteria. Such differences are almost never discernible in published reports. The possibility that these factors accounted for the DSTs diagnostic non-specificity in some studies led us to predict that diagnoses modified by prospective observations would more closely correspond to neuroendocrine test results.

Methods

An earlier paper (Coryell and Zimmerman 1986) described intake and baseline diagnostic procedures in detail. Briefly, consecutively admitted patients at the University of Iowa Psychiatric Hospital were invited to participate if they had a functional nonmanic psychosis and had none of the features thought to invalidate either the DST or the thyroid releasing hormone

Offprint requests to: W. Coryell

stimulation test. The second author, MZ, reviewed all available records before administering the full Schedule for Affective Disorders and Schizophrenia (SADS, Endicott and Spitzer 1978), always within 1 week of admission. The first author, WC, independently reviewed records and conducted an unstructured interview to arrive at axis I diagnoses. MZ and WC then met to reach diagnostic consensus according to the Research Diagnostic Criteria (RDC, Spitzer et al. 1978). Disagreements were frequent and a consensus often required further interview of the patient or reading of available records. The study design did not provide for recourse to a third party at this point. Through this process, we identified within 1 week of admission 97 patients who met criteria for major depression, schizoaffective disorder, depressed-type, or schizophrenia.

Patients also underwent neuroendocrine assessments within a week of intake. The DST component consisted of 1 mg taken orally at 11:00 p.m. with plasma collections the following day at 0800 and 1600 h; 61.9% of the patients submitted 2300 h samples as well. The conventional threshold of 5 μg/dl best separated patients with major depression from controls who lacked either a personal or family history of psychiatric illness (Coryell and Zimmerman 1987a); therefore patients with a value of >5 μg/dl on any sample were considered baseline nonsuppressors.

We were able to reinterview 86 (88.7%) of these patients at both 6-month and 1-year intervals. At each interview MZ quantified, on a week by week basis, all psychopathology occurring in the previous 6 months. In particular, he rated all symptoms comprising the criteria for the RDC major affective disorders or for schizophrenia. All inpatient and outpatient records, both from this and from other facilities, were sought, reviewed, and incorporated in these ratings.

After the 12-month follow-up, MZ reconsidered the baseline diagnosis in light of all psychopathological developments since intake. At the same time, a senior clinician, GW, reviewed medical records (both predating and postdating intake), the SADS interview, the baseline consensus diagnosis and both follow-up interviews; he then independently determined a diagnosis. MZ and GW then met to reach a consensus on the follow-up diagnoses. In 25.6% of cases MZ and GW disagreed; these were reviewed by yet another senior clinician, RC, who assigned a final diagnosis. MZ, GW, and RC remained blind to neuroendocrine results throughout.

Results

We identified at baseline 26 patients with major depression, psychotic-type, 46 with schizoaffective disorder, depressed-type, and 21 with schizophrenia. The first report from this series (Coryell and Zimmerman 1987a) compared these groups by demographics and phenomenology.

We completed 6- and 12-month follow-ups for 100%, 91.3%, and 85.7% of the major depression, schizoaffective, and schizophrenia patients, respectively. Approximately one-fourth of the patients with a baseline diagnosis of schizophrenia or major depression were given follow-up diagnoses of schizoaffective disorder.

The DST results at intake corresponded to follow-up diagnoses much more clearly than to intake diagnoses (Table 1). In particular, specificity to a nonschizophrenia diagnosis increased from 66.7% to 84.6% while the positive predictive value (the likelihood that a positive test indicated a nonschizophrenia condition) increased from 62.2% to 94.6%. Of the 6 patients with a baseline diagnosis of schizophrenia and a positive DST result, 4 (66.7%) were rediagnosed on follow-up; of patients with a baseline diagnosis of schizophrenia and a negative DST result, only 1 (8.3%) was rediagnosed ($P=0.02$, Fisher's exact test).

Table 1. Baseline dexamethasone suppression test results and diagnostic stability during a 1-year follow-up

	N	No. (%) non-suppression
Patients grouped by		
– Baseline diagnosis		
Schizophrenia	18	6 (33.3)
Schizoaffective depression	42	17 (40.5)
Major depression, psychotic	26	14 (53.8)
– Diagnostic change		
Schizophrenia to schizoaffective depression	5	4 (80.0)
Major depression, psychotic to schizoaffective depression	7	2 (28.6)
– Follow-up diagnosis*		
Schizophrenia	13	2 (15.4)
Schizoaffective depression	54	23 (42.6)
Major depression, psychotic	19	12 (63.2)

* Schizophrenia vs major depression by baseline nonsuppression rate, $\chi^2=7.2$, 1 *df*, $P<0.01$

Discussion

The relationship between diagnosis and baseline DST results were much more apparent after a year of prospective observation. Specifically, nonsuppression at baseline was clearly associated with diagnostic instability among schizophrenic patients.

The study's design determined, to a large extent, the direction of diagnostic change. Unlike studies of diagnostic reliability over time, follow-up diagnoses here were determined with full knowledge of baseline groupings; the intent was to generate a more valid diagnosis rather than to test reliability. This fact and the structure of the RDC made diagnostic changes, other than those observed here, unlikely. A change from major depression or schizoaffective disorder to schizophrenia, for instance, would require that the patient recover from the index episode (ex-

perience 2 months without symptoms) and then develop psychotic features in the absence of an affective syndrome. A shift from schizophrenia to major depression would, likewise, require recovery and the appearance of a new episode quite different from the preceding one. The lack of such changes in the present study was therefore not surprising given a follow-up length of only 1 year. Instead, all changes were toward schizoaffective disorder, a category marked by fundamental heterogeneity (Coryell 1986) and one which appropriately overlaps much of the group labeled undiagnosed in an earlier diagnostic system (Coryell and Zimmerman 1987b).

A 5-year follow-up is underway and will show us whether those schizophrenics rediagnosed as schizoaffective disorder assume a course which more and more resembles affective disorder; those DST suppressors whose diagnoses shifted from major depression to schizoaffective disorder alternatively may assume a long-term course progressively more indicative of schizophrenia. If so, the DST as used here, or appropriately modified, might be useful in purifying schizophrenic samples used in research. In clinical settings, DST nonsuppression might be cause for a review and further gathering of historical material possibly indicative of affective disorder. In any case, these findings show that the biological correlates of psychoses may best be studied when diagnostic uncertainty is acknowledged and then lessened through prospective reevaluations.

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