The use of the dexamethasone suppression test in the evaluation of depression: A re-examination

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The clinical and research usefulness of the dexamethasone suppression test (DST) in diagnosis of endogenous depression has become the subject of considerable controversy. Following the original report on the standardization of this test, subsequent studies often deviated in significant ways in methodology. The present study of 107 subjects was undertaken to determine the specificity and sensitivity of the DST utilizing a methodology similar to that of the original report. The sensitivity of the DST was 57 percent for definite endogenous depressive disorder and 7 percent for nonendogenous depression. The specificity and predictive value of the DST for endogenous depression were 82 percent and 89 percent, respectively. These results are quite comparable to those of the original standardization study. These data support the validity of the DST as a biologic marker for endogenous depression, and, when properly utilized, the test can be an effective adjunctive tool for confirming the clinical diagnosis of this disorder.

The clinical and research utility of the dexamethasone suppression test (DST) in psychiatry recently has become quite controversial. Abnormal cortisol secretion, as measured by the DST, has been thought by some researchers to be a biologic marker of melancholic depression. The clinical diagnosis of melancholic depression is made when the history and examination of the patient reveal a

combination of such symptoms as a depressed mood distinct from grief, lack of reactivity, diurnal mood variation, loss of interest and pleasure, feelings of guilt or self reproach, early morning waking or middle of sleep insomnia, psychomotor retardation or agitation, poor appetite, and nondieting weight loss.¹ While some believe that this diagnosis can be aided by appropriate laboratory testing, with the DST having reasonable predictive capabilities in a preselected population,² other authors³⁻⁵ have questioned the sensitivity and specificity of the test.

Most of the controversy surrounding the applicability of the DST in the clinical evaluation of depression has focused on its specificity. Several researchers have challenged Carroll and associates² report of a 96-percent specificity rate for melancholic depression with their own findings of abnormal cortisol secretion in patients with primary degenerative dementia,⁶ panic attacks,⁷ nonmelancholic depression,⁵ separation anxiety disorders of childhood,⁸ bulimia,⁹ schizophrenia,^{3,4} and abstinent alcoholism.⁵

There are two major difficulties in comparing information among DST studies. First, many of the studies that suggested that abnormal cortisol secretion is not specific to melancholic depression have used small sample sizes. Second, no uniform research methodology was used in the respective studies; the methodologic differences include different diagnostic classification systems for assigning patients to research groups as well as varying procedures for patient exclusion.

The purpose of the present study was to determine the cortisol suppression rates for endogenous and nonendogenous depression in an independent, large sample of patients using classification and exclusion procedures similar to those employed by Carroll and associates.²

Subjects and methods

Patient selection

The subjects for the present study consisted of 107 patients who presented with a chief complaint of depression at a consortium of outpatient and inpatient psychiatric facilities in a large, Midwestern university. The demographic characteristics of the patient sample are displayed in Table 1. Patients' ages ranged between 18 and 65 years. All but 6 of the subjects were seen on an outpatient basis, and all were free of medical illnesses and medications that were reported by Carroll and associates² to invalidate the DST. Exclusion criteria also included a history of bipolar depression or concurrent diagnosis of alcoholism, schizophrenia, organic brain syndrome, or anorexia nervosa. Socioeconomically, this group of subjects primarily was middle classed. Diagnostically, subjects met the criteria for one or more categories for primary depression (Table 2).

Rater training and assessment of clinical features

The interviewer/raters for this project were trained

using materials and procedures drawn from a training program specifically developed for the Research Diagnostic Criteria (RDC) program.¹ A complete discussion of the training procedures and results has been provided elsewhere.¹⁰ Patients were assessed for current symptomatology using Part I of the Schedule for Affective Disorders and Schizophrenia (SADS),¹¹ a semistructured interview for psychiatric disorders. They then were diagnosed according to the RDC.

Dexamethasone suppression testing

Following the diagnostic interview, each subject was given the DST. Each subject received 1 mg. of dexamethasone orally at 11 p.m., and a single blood draw was performed at 4 p.m. the next day. Cortisol sampling at 11 p.m. was omitted to avoid inconvenience for this mostly outpatient group. Plasma cortisol levels were assayed using a GammaCoat (¹²⁵I) radioimmunoassay kit (Clinical Assays). The assay was compared periodically during the study with the competitive protein-binding procedure of Carroll's group.² While there was some variation across lot numbers of the radioimmunoassay kit, for the entire sample a cortisol level of 4.6 µg./dl. found with GammaCoat (¹²⁵I) was equivalent to 5.0 µg./dl. using competitive protein binding. Therefore, in the current study, a serum cortisol level > 4.6 µg./dl. was used as the criterion for cortisol nonsuppression.

Time period for analysis

SADS item ratings for the week prior to evaluation were used for the statistical analyses in this study. The decision to select the most immediate severity ratings of clinical features was based on the hypothesis that DST nonsuppression is a transitory variable, whose possible clinical concomitants are most likely to be identified when DST response and clinical phenomenology are measured within a close time frame.

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF STUDY POPULATION.

Sex	Male (n = 30)	Female (n = 77)
Diagnosis		
Definite/probable endogenous depression	19	50
Nonendogenous depression	11	27
$X^2 = 5.932, p = .014$		
Age	Number of patients	Mean (years)
Diagnosis		
Definite/probable endogenous depression	62	40.70
Nonendogenous depression	45	35.97
$t \text{ value} = -2.17, p = .031$		
Severity*	Number of patients	Mean
Diagnosis		
Definite/probable endogenous depression	62	21.09
Nonendogenous depression	45	13.65
$t \text{ value} = -5.74, p = .0001$		

*As determined by mean Hamilton Depression Rating Scale Score

TABLE 2. DIAGNOSTIC PERFORMANCE OF DST ACCORDING TO RDC CATEGORIES.

Category	Number of subjects (total = 107)	Prevalence (percent)	Positive DST (number)	Sensitivity (percent)	Specificity (percent)	Predictive value (percent)
Major depressive disorder (MDD)						
Definite and probable	82	77	25	30	92	92
Definite	64	59	22	29	88	
Probable	18	17	3	17	73	
Endogenous MDD						
Definite and probable	62	58	24	39	82	89
Definite	30	26	17	57	81	
Probable	32	31	7	22	76	

Results

Response to dexamethasone

Twenty-seven patients failed to suppress normally on the DST, with 24 having cortisol values > 5.0 $\mu\text{g./dl.}$ Of the 80 suppressors in the study, 63 had cortisol values ≤ 2 $\mu\text{g./dl.}$, 9 between 2.1 and 3.0 $\mu\text{g./dl.}$, and 8 between 3.1 and 4.0 $\mu\text{g./dl.}$

Table 2 presents the nonsuppression rates for each RDC diagnostic category. The sensitivity of the DST (53 percent [16/30] for definite endogenous depression, 25 percent [8/32] for probable endogenous depression, and 7 percent [3/45] for nonendogenous depression [nonendogenous major, intermittent, or minor depressive disorder]) was comparable to those reported by Carroll and associates.²

The specificity and predictive value of the DST for probable and definite endogenous depression (82 percent and 89 percent, respectively) determined in the present study also are comparable to those reported by Carroll's group.²

Table 3 demonstrates the nonsuppression rate for various RDC subgroups. Interestingly, 24 percent (20/82) of our subjects with RDC major depressive disorders were nonendogenous. Again, this finding was quite comparable with the 31 percent reported by Carroll and associates.²

In terms of treatment response in the endogenous group, 10 of 13 DST nonsuppressors (77 percent) responded to desipramine, while 10 of 21 suppressors (48 percent) experienced a favorable response. This difference fell just short of statistical significance. These data are being prepared for publication in more detail.

Conclusions

These data support the validity of the DST as a biologic marker both for major depressive disorder and endogenous depressive disorder. While the specificity of the DST was similar among four categories (MDD [definite and probable], MDD [definite], endogenous MDD [definite and probable], and endogenous MDD [definite]), the sensitivity of this test was highest in the definite endogenous group. It is important to note that only 4-p.m. cortisol levels were determined. The addition of 11-p.m. samples would be expected to increase sensitivity somewhat. The high percentage of endogenous subjects included in this study reflects prescreening that occurred prior to evaluation for the protocol.

These data are strikingly similar to the results reported by Carroll and associates.² While both of our research centers are located in Michigan, the authors of this article believe that the similarity in our data reflects the similar application of diagnostic criteria and the use of similar methodology

TABLE 3. FREQUENCY OF ABNORMAL DST RESULTS IN RDC SUBGROUPS.

Diagnosis	Number of subjects	Positive DST	
		Number	Percent
Major depressive disorder (MDD)			
Definite and probable	82	25	30
Definite	64	22	34
Probable	18	3	17
Endogenous MDD			
Definite and probable	62	24	39
Definite	30	17	57
Probable	32	7	22
Nonendogenous disorders			
Intermittent depressive disorder	12	0	0
Minor depressive disorder	13	2	15

(that is, exclusion criteria and cortisol assay procedure). We believe that much of the controversy regarding the validity of the DST has been generated from studies utilizing methodologies that differed from those of Carroll's group. It is also interesting to note that our sample size is large as compared to those of many DST studies.

In addition to the cross-sectional studies to date, further studies that include family history, course over time (including serial diagnoses), history of treatment response, and correlation with other biologic markers clearly are necessary.¹² Nonetheless, we believe that the DST can be a useful, adjunctive tool for confirming the clinical diagnosis of endogenous depression. These data, combined with those from studies¹³⁻¹⁶ demonstrating a more favorable response to somatic treatments among DST nonsuppressors, suggest that depressed patients most likely to respond to antidepressant medication are those with both a clinical diagnosis of endogenous depression and an abnormal response to the DST. Additional studies of the efficacy of the DST in monitoring response to treatment, in predicting relapse, and in predicting suicide hopefully will resolve the controversy regarding the role of this laboratory test in psychiatry.^{12,17}

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