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Neurotic Depression: a Diagnosis Based on Preexisting Characteristics

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Summary. A neurotic depression is a depression in an emotionally unstable person. Secondary depressions to major personality disorders, neuroses, and drug use disorders fit the above definition. Likewise, primary depressions with a family history of alcohol (depression spectrum disease) are characterized by a long history of stormy life problems and, therefore, would fit the definition. Using these two preexisting characteristics, we examined a group of 401 neurotic depressives and compared them to 536 nonneurotic (endogenous) depressives. The neurotic depressives were younger and the neurotic patients had made more previous suicide attempts. They were less likely to show memory deficits or delusions and less likely to show symptom criteria of melancholia. They were more likely to have suicide thoughts at index. Treatment was more effective in the nonneurotic patients and such patients made fewer suicide attempts in follow-up. These differences confirm the validity of the distinction between neurotic and nonneurotic depression.

Key words: Neurotic depression – Diagnosis – Preexisting characteristics

Introduction

An ordinary dictionary definition of a neurotic is an emotionally unstable individual. A definition of neurotic-reactive depression would include those patients who suffer from a depression in the context of chronic gross personality problems and a history of a stormy lifestyle. One of the most venerable debates in psychiatry has been whether patients with neurotic-reactive depressions deserve to be considered as suffering from a separate illness or disease when compared to those patients who suffer from an "endogenous depression". The terms neurotic depression and reactive depression have often been used synonymously, but the fact is that depressions reactive to life stresses may be entirely different from those depressions that occur in the context of an unstable personality and a stormy lifestyle, i.e., a "neurotic depression". A person suffering from a neurotic depression may have little in common with a person who suffers a depression as a reaction to a life stress. Life stress as an etiological factor in depression has really not been able to separate patients with neurotic and endogenous depressions. It may be that a precipitating factor in depression may not be very important in defining the "nonendogenous" group. Paykel (1979, 1982) suggested that precipitating factors were seen in all kinds of depression. Precipitated depressions (reactive) showed few differences in symptoms from unprecipitated depressions (presumably endogenous).

Recent work on "situational" depression is relevant to this discussion. A situational depression is a depressive illness which developed after an event or in a situation which seemed likely to have contributed to the appearance of an episode at that time (Hirschfeld et al. 1985). A comparison of situational major depressions with nonsituational major depressions showed no difference in clinical characteristics or family history. Interestingly, the presence of precipitating events did not distinguish responsiveness to imipramine or electroconvulsive therapy (ECT) in a large treatment study (Avery and Lubrano 1979). Alternatively, the concept of neurotic depression may be quite useful. This is a depression that occurs in the context of a stormy lifestyle and an unstable personality with or without the presence of precipitating factors. There are a variety of synonyms that might be used. These include chronic characterologic depression, character spectrum disorder, and conflictual depression (Winokur 1985). We have chosen to use the term "neurotic" because it is classic term that has been used in the past and also has a perfectly acceptable dictionary definition.

In fact, if we accept the term "neurotic depression" as indicating a depression in an individual with an unstable personality and a stormy lifestyle, it may be fitted to two other diagnoses. A secondary depression would also fit the definition of a neurotic depression, particularly if that secondary depression were secondary to such psychiatric illnesses as alcoholism, drug abuse, somatization disorders, anxiety disorders, and personality disorders, including antisocial personality. All of these diagnoses would be associated with an unstable personality and considerable conflict with the environment. The other diagnosis which would fit the concept of neurotic depression would be that of depression spectrum disease which is a depression in an individual who has a family history of alcoholism. The reason that neurotic depression and depression spectrum disease appear similar is that primary depressives with a family history of alcoholism (depression spectrum disease) show lifetime personality problems and a stormy lifestyle (Winokur 1985). Such patients when compared to depressives who have no family history of alcoholism are more likely to have received a clinical diagnosis of neurotic-reactive depression, more likely to have shown lifelong characteristics of fear, demanding behavior, need for reassurance, nervousness, complaining, and irritability, and are more likely to show evidence of stormy life events such as divorce, separa-

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tion, and sexual problems (Winokur 1979). Several studies show a relationship between a clinical diagnosis of neurotic depression and a family history of alcoholism (Winokur 1985). Pfohl et al. (1984) separated patients who had a depression into those with and without personality disorder and those patients who had a diagnosable personality disorder were significantly more likely to have a family history of alcoholism. Recent research by Price and Nelson (1986) is relevant. These investigators examined the family history of psychiatric illness in first-degree relatives of depressives. Morbid risk for a alcoholism in the relatives of unipolar, nonmelancholic probands was 16% as compared to 5% in the relatives of unipolar melancholic probands. Further, the presence or absence of delusions was related to a different morbid risk for alcoholism, 7% in the relatives of nondelusional patients versus 2% in relatives of delusional probands. Thus, the diagnosis of nonneurotic or endogenous depression is associated with a deficit of alcoholism in family members when compared to the nonmelancholic, nondelusional patients.

Secondary depression occurs in an individual who has another psychiatric illness which predates the onset of the depressive syndrome. By defining neurotic depression as a depression superimposed on a gross personality disorder of a neurotic nature or on an unstable personality, secondary depression meets the requirements for the diagnosis. Recent data from a large multicenter study (Collaborative Depression Study) indicate that secondary depressives are more likely than primary depressives (those patients with only a diagnosis of depression and nothing else) to have a diagnosis of alcoholism in their relatives (Grove et al. 1987). Likewise, they are more likely to have a diagnosis of secondary unipolar depression in their relatives than are those with primary depression. This, of course, is expected because secondary depression is a common syndrome in patients with other primary illnesses. For example, 44% of patients who meet criteria for anxiety neurosis are likely to have a diagnosis of secondary depression (Clancy et al. 1978). When one evaluates alcoholism in relatives of secondary depressives whose primary diagnoses are anxiety disorders, somatization disorders, or drug abuse (excluding primary alcoholic probands with secondary depression), one again finds an increase in alcoholism as compared to alcoholism in the relatives of primary depressives. Likewise, relatives of primary depressives are less likely to have a diagnosis of phobic disorder and generalized anxiety disorder than are relatives of alcoholics with secondary depression. Recent studies of anxiety disorders show a significant increase in the morbid risk for alcoholism in family members as opposed to the family members of controls (Harris et al. 1983). Thus, there are a number of familial relationships relevant to neurotic depression as we have defined it (Winokur in press).

These are: (1) secondary depression is more frequent in relatives of secondary depressives than relatives of primary depressives; (2) primary depression is seen equally in relatives of secondary and primary depression; (3) alcoholism and drug abuse are seen equally in relatives of alcoholic secondary depressives as in relatives of other secondary depressives (excluding alcoholics); (4) phobic disorder is seen more frequently in relatives of alcoholics with secondary depression than in relatives of primary depressives; (5) alcoholism is seen more frequently in relatives of panic disorder patients than in relatives of controls; (6) depressed patients with hysterical personality are more likely to have alcoholic fathers than depressed patients without hysterical personality (Lazare and Klerman 1968); (7) both clinical and research diagnoses of neurotic-reactive depression are associated with more familial alcoholism than are diagnoses of endogenous depression; and (8) in patients with depression and personality disorder familial alcoholism is more frequent than in patients with depression and no personality disorder. Thus, we are left with the concept of neurotic depression being related to a variety of other illnesses in psychiatry both as a primary illness (depression spectrum disease) as well as illnesses secondary to neuroses, substance abuse disorders, and personality disorders.

Using the concept of neurotic depression as a diagnostic entity that is composed of either depression secondary to neuroses, personality disorder or substance abuse disorder or primary depression with a family history of alcoholism, we compared such patients with those depressives that fit neither of these two categories. These two categories were called "neurotic depression" and "endogenous depression" but in fact endogenous depression is for practical purposes a depression left over by exclusion of the neurotic depressives. This neurotic depression group was composed of secondary depressives plus depression spectrum patients, primary depressives with a family history of alcoholism. These were added together because both fit the definition of neurotic depression, i.e., a person who suffers a depression superimposed on an unstable personality with stormy life events. The goal of this paper was to determine whether neurotic depression so defined shows differences in clinical, treatment, and course characteristics from nonneurotic or endogenous depression.

Methods

The patients in this study were culled from 2,054 patients admitted to the University of Iowa Psychiatric Hospital between January 1, 1970 and December 31, 1981. These patients had chart diagnoses of either unipolar depression, bipolar disorder, manic disorder, involutional melancholia, manic depressive psychosis, atypical depression, atypical bipolar, atypical psychosis, schizoaffective disorder, secondary depression, neurotic depression, cyclothymia, or dysthymia.

The 2,054 medical records were systematically evaluated and the following items were coded: sex, marital status, age at index admission of previous hospitalizations, age at index hospitalization, duration of illness at admission, precipitating events, organic features at admission, suicidal thoughts at admission, the presence of melancholia symptoms at index admission, delusions and hallucinations, treatment and response during index hospitalization, previous treatments and response, previous suicide attempts, outcome at discharge, death including cause of death and relapse after discharge, and specific family histories of alcoholism and depression.

To obtain the sample for this study, we eliminated all patients with an organic brain syndrome or a diagnosed medical disorder. Likewise we excluded all patients that had any kind of bipolar disorder, atypical disorder or schizoaffective disorder. Thus, we were left with 937 patients who met the DSM-III criteria for major depression, single episode or recurrent episode. We divided these patients into two groups. The first was a group which we call "neurotic" depression; it contained patients who in addition to having a major depression had another preexisting diagnosis such as substance abuse, anxiety disorder, simatization disorder, personality disorder, or anti-

social personality disorder. To complete the group of neurotic depressions, we added all primary depressives who had a diagnosis of major depressive disorder and a family history of alcoholism. This combined group numbered 401 patients. The remainder which we call the endogenous depression group numbered 536.

Having separated the two groups, they were compared on the variables which were coded out. The groups were evaluated statistically using χ^2, and for continuous variables t-tests were used.

Results

There were 536 patients who were considered endogenous and 401 patients who were considered neurotic. Of the neurotic patients, 170 filled the criteria of primary depression with a family member who was alcoholic (depression spectrum disease); 231 patients were secondary to other disorders. Of those with secondary depressions, 72 were secondary to substance abuse, 41 were secondary to anxiety disorders, 23 were secondary to somatization disorders, 78 were secondary to nonantisocial personality disorders, and 17 were secondary to antisocial personality. A total of 50 statistical comparisons between the neurotic and endogenous groups were made.

Table 1 shows some of the clinical characteristics which separated the groups. The neurotic patients were younger at index, more likely divorced or separated, and less likely to have been hospitalized at index for the first time. They became ill at a younger age and they had more previous suicide attempts. Equal proportions of the neurotic and endogenous patients had had a previous depressive episode, 60% vs 63%.

Symptom differences are presented in Table 2. A memory deficit was noted on index mental status more frequently amongst the endogenous patients; and those patients were also more likely to be delusional and fill the melancholia symptom criteria of DSM-III. The neurotic patients were more likely to show suicide thoughts at the index admission.

As regards course and treatment, the groups were quite different. The neurotic patients were hospitalized for a shorter period of time, less likely treated with neuroleptics, less likely to have shown marked improvement when treated with ECT, more likely to have had no somatic therapy of any kind, more likely to have been discharged on no maintenance antidepressant, less likely to have been markedly improved at discharge, and more likely to have made suicide attempts during hospitalization or follow-up.

Among the comparisons that were not significantly different were state of residence, the presence of precipitating events, hallucinations, antidepressant treatment at index, use of more than one antidepressant at index episode, dosage of antidepressants, duration of antidepressant use at index episode, lithium at index episode, lithium blood level at index episode, the presence of marked improvement or improvement with antidepressant therapy, and antipsychotic maintenance therapy following hospitalization. Notably, there was not even a trend toward a better antidepressant response in the endogenous patients over the neurotic patients. The duration of follow-up was not significantly different and there was no difference in relapse after discharge.

There was a trend for an increased number of endogenous patients to have committed suicide postdischarge ($\chi^2 = 3.49$, $df = 1$, $P < 0.1$, 2-tailed) but only for the short term follow-up (up to 1 year). By the end of the follow-up time, which was the same for the two groups, an equal number of patients had committed suicide (4%) in both the neurotic and endogenous groups.

A dexamethasone test was performed in 126 endogenous patients and 102 neurotic patients; the postdexamethasone cortisol level was tested at 8a.m. The mean postdexamethasone cortisol for the endogenous group was $5.9 \pm 6.3\,\mu g/dl$ as opposed to $2.5 \pm 4.1\,\mu g/dl$ in the neurotic group. The difference was significant at the 0.0001 level. In 86 endogenous patients

Table 1. Clinical characteristics

	Endogenous	Neurotic	P
n	536	401	–
Female	64%	64%	N.S.
Age at index, mean ± SD	46 ± 18	38 ± 15	0.0001
Divorced or separated	59 (11%)	82 (20%)	0.0005
Index admission – 1st hospitalization	168 (31%)	100 (23%)	0.05
First ill before age 20	70 (13%)	131 (33%)	0.0005
Depressed prior to hospital < 6 months	202 (38%)	180 (45%)	0.05
Previous suicide attempts	161 (30%)	184 (46%)	0.0005

Table 2. Symptoms

	Endogenous	Neurotic	P
n	536	401	
Memory deficit	73 (14%)	33 (8%)	0.01
Suicide thoughts at index	221 (41%)	204 (51%)	0.005
Delusions	91 (17%)	38 (9%)	0.001
Fills melancholia symptom criteria of DSM-III	87 (17%)	28 (7%)	0.0005

Table 3. Course, treatment, and follow-up

	Endogenous	Neurotic	P
n	536	401	
Duration of index hospitalization less than 4 weeks	283 (53%)	255 (64%)	0.001
Treatment with neuroleptics at index	114 (21%)	62 (15%)	0.02
Marked improvement in those treated with ECT	158/264 (60%)	49/114 (43%)	0.005
No somatic therapy of any type	13%	24%	0.0005
No maintenance antidepressant	28%	39%	0.0005
Discharged as markedly improved	336 (63%)	194 (48%)	0.0005
Suicide attempts in hospital or after discharge	16 (3%)	25 (6%)	0.005

and 67 neurotic patients, where the postdexamethasone cortisol level was tested at 4 p.m., the endogenous group had a mean of 6.0 ± 6.3 μg/dl vs neurotic 3.7 ± 4.4 μg/dl. This difference was significant at the 0.009 level.

Discussion

All the patients in this study met DSM–III criteria for major unipolar depression. Using an operational definition of neurotic depression which combines two groups of patients (those who have a primary depression with a family history of alcoholism plus those who have a secondary depression to personality disorders, drug use disorders or neurotic disorders), we found highly significant differences from those patients which constituted the remainder of primary depressions (endogenous). These validators were all in the direction of the differences in the literature on neurotic depression which is defined as an illness occurring in a person with a stormy lifestyle and marked lifelong personality problems. The neurotic patients were more likely to have marital problems, and less likely to respond to hospitalization with marked improvement. The endogenous group was more likely to have melancholia symptoms and to have had such psychotic symptoms as delusions and to have memory problems on mental status examination. The methodology enabled us to separate two groups at a high level of significance, but what is clear from the findings is that there is no pathognomonic sign or symptom to separate endogenous from neurotic: the overlap is large. The value of the definition of neurotic as the combination of the two other diagnoses is in the fact that it is not based on the clinical picture itself primarily but rather on either a family history or what happened in the past, things which in themselves cannot be considered influenced by the fact that the person had a depression at the time of study. The depression at index could not have influenced either the past behavior or the family history. This supports the validity of the concept of neurotic depression as defined in this paper.

The methodology is of interest because unlike a number of current investigations the emphasis was on the neurotic group rather than the endogenous group. The endogenous group was simply defined as the remainder after we had combined the depression spectrum patients and the secondary depressives. Many recent studies started with an attempt to define a group of endogenous depressives according to the clinical picture and used the neurotic group as the exclusion patients. Because the definition of depression subtype used in this paper was related to things that have occurred far in the past and things that have been stable over a period of time, we believe that an appropriate algorithm should start by separating the neurotic depressives and dealing with the remainder rather than starting with the endogenous as the nuclear group.

Other comparisons of endogenous and neurotic depression have been published, and one is of particular interest. Kendell (1968) studied 1,080 patients who had been admitted to the Maudsley Hospital. He utilized a discriminant function analysis and examined 60 items. A bimodal distribution should have been found if psychotic (endogenous) and neurotic depression were distinct illnesses; and since such a distribution did not occur, Kendell suggested that depressive illnesses should be considered a single continuum, extending between the traditional neurotic and psychotic stereotypes. The lack of bimodality may be the result of the patients being severely ill and thus sharing the kinds of symptoms which necessitate hospitalization. Further, 30% of Kendell's items did not discriminate between groups and putting those into the analysis could obscure bimodality. An interesting exercise would be to use only the family history, previous personal history, history of present illness and etiology (precipitants) of the present episode for the discriminant function analysis. Certainly the types of symptoms used in a discriminant function analysis should affect the results. The mental status findings themselves may have little resolving power. Kendell's data are interesting in another way. The neurotic depressive group was more likely to show childhood neurotic traits, previous hysterical symptoms, previous subjective tension symptoms, previous demonstrative suicidal attempts, previous serious suicide attempts and to be always ailing. The nonneurotic group had previous similar episodes and obsessional symptoms. These same kinds of items, in general, separated our two groups but in the the present study the dichotomy started at the beginning where specific definitions were given for neurotic and endogenous depression. Another difference between Kendell's study and ours is that we have presented data on course of illness and response to treatment and, in fact, the separately defined groups differed considerably for these variables.

There was another set of data which separated the neurotic from the endogenous depressives in this study, the dexamethasone suppression test results. These data are somewhat flawed in that two methods were used to determine postdexamethasone cortisol level. Some tests used a radioimmunoassay method and others a protein binding method. These two methods have sometimes been associated with different threshold points as to what might be called abnormal. We present a significant difference between the two groups in this paper; but by using a more conservative definition of suppressor status (i.e., <1.5 μg/dl for normal and >6.0 μg/dl being abnormal) we have been able to demonstrate that abnormal endocrine function is related to specific kinds of depressive symptoms (Winokur et al. 1987). Melancholic symptoms, delusions, and memory deficit were associated with the endogenous depressives and abnormal suppressor status (>6.0 μg/dl). Early onset, and poor response to treatment were associated with the neurotic depressives and normal suppressor status (<1.5 μg/dl). The definition of neurotic depression was the same as in the present paper.

Shagass (1981) reviewed the neurophysiological evidence for the existence of different types of depression. In particular, he concentrated on the controversy between neurotic versus psychotic depression. His review of the evidence supported the discontinuity position and he concluded that more than one process underlies clinical depression. Of the discriminators between psychotic and neurotic depression, Shagass cited a large number which included response to ECT, salivary secretion, blood pressure response to mecholyl, sedation threshold using both EEG and galvanic skin responses to end point, stimulation threshold, sleep EEG and rapid eye movement (REM) latency, growth hormone response to amphetamine, clonidine, desipramine, or insulin, the dexamethasone suppression test, and evoked cortical potentials. Of course, the definition of neurotic and psychotic depression in these studies differs widely. Using the definition of neurotic depression in the present paper, we should ask whether there would be differences in neurobiological test results when depression spectrum disease patients were compared with other types of depression or when secondary depressives were com-

pared with other types of depression. Winokur (1986) reviewed the separation between familial pure depressive disease and depression spectrum disease, the former being similar to endogenous depression, the latter similar to neurotic depression. There was a consistent difference in the dexamethasone suppression test with the familial pure depressives (endogenous depressives) being nonsuppressors and the depression spectrum patients (neurotic depressives) normal suppressors. There were also differences between the depression spectrum patients and familial pure depressives in glucose sensitivity to insulin, imipramine binding platelet membranes, REM latency, diurnal advance of cortisol nadir, and response to somatic treatment. Yerevanian and Akiskal (1979) studied shortened REM latency in depressives and found that the primary depressive group showed this phemenonon whereas the group of secondary depressives to nonaffective psychiatric illnesses were normal as regards the REM latency measure. Schlesser et al. (1980) and Coryell et al. (1982) showed evidence that primary depressives were likely to be abnormal nonsuppressors to the dexamethasone suppression test whereas secondary unipolar depressives were likely to be normal suppressors. Neurotic depressives were different from psychotic or endogenous depressives in laboratory tests; and if one evaluates depression spectrum disease patients, they were different from familial pure depressives and secondary depressives were different from primary depressives. In all of these cases, neurotic depression, secondary depression, or depression spectrum disease, the laboratory findings were close to normal controls; the endogenous or psychotic or familial pure depressives appeared abnormal.

The consept of a secondary depression includes the possibility that a depression could be secondary to such illnesses as organic brain syndromes, schizophrenia, and medical illnesses. In fact, we evaluated depression secondary to medical illnesses (Winokur G, Black D, Nasrallah A (1987) Depression secondary to other psychiatric disorders and medical illness, submitted for publication). There are marked differences in secondary depressions which occur after the onset of medical illnesses from those which occur after the onset of a neurosis, substance abuse disorder, or personality disorder. The depressions secondary to medical illnesses are older at onset, less likely to be accompanied by suicide thoughts and previous suicide attempts, and more likely to be associated with memory problems. In follow-up those patients who are secondary to a medical illness show more improvement with treatment and are less likely to relapse. Further, the family histories of those depressions secondary to medical illnesses show less alcoholism than those patients who have secondary depressions to psychiatric illnesses even when the secondary depressions to alcoholism have been excluded. These data suggest that depression secondary to substance abuse disorders, neuroses, and personality problems fit the concept of "neurotic depression" in that they occur in the context of a long history of stormy life events and problems. On the other hand, those patients who have depressions secondary to serious medical illnesses seem to fit the concept of a "reactive depression" in that they occur late and in the context of no previous psychiatric difficulties.

Finally, these data are in favor of the idea that the criteria for depression as we now know them in DSM-III or the Feighner Criteria, or the RDC do not define a disease but a syndrome (DSM-III 1980; Feighner et al. 1972). All of the patients in this study met the criteria for a major depression according to DSM-III and all were hospitalized. This syndrome can result from a variety of many circumstances. When the syndrome occurs in the context of a long standing psychiatric condition manifested by a stormy lifestyle and personality problems, it may be called a "neurotic" depression. It occurs frequently under these circumstances. Some patients do not meet reasonable criteria for a primary illness but only show a stormy lifestyle and personality problems which are not diagnosable. These are patients we consider to have a primary depression but have a family history of alcoholism (depression spectrum disease). As time goes on and we are better able to diagnose personality syndromes with some degree of reliability, we may consider all neurotic depressions as secondary depressions to some kind of primary neuroses, drug use disorders, or personality disorders. Until that time we might simply combine the two groups to compose our neurotic depressive category.

The algorithm which would be used is as follows: unipolar depression would be divided into unipolar and bipolar on the basis of a lifetime history. The unipolar depression would be separated into secondary and primary. The primary depressives would be separated into familial subtypes, depression spectrum disease (a depression with a family history of alcoholism and/or social personality with or without a family history of depression), familial pure depressive disease (a family history of only depression), and sporadic depression (a depressive patient with a family history of no other psychiatric illness). Then the secondary depressives and the depression spectrum disease patients would be combined to make a neurotic depressive subgroup. This subgroup would be a comparison group to the remainder of the unipolar depressives.

The value of separating the neurotic from the endogenous depressives has meaning for subsequent research. At the very least, the patients with depression spectrum disease and secondary depression should be removed from the large mass of depressives in order to obtain a more restricted and pure group for further research. Already, we know that spectrum patients and the secondaries are different from the familial pure depressives and the primary depressives. To include them in any subsequent study of treatment or abnormal markers may well lead to rejecting a hypothesis when, in fact, it is true (a type 1 error).

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