Suicide Attempters, Nonattempters, and Neurotransmitters

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NINETY-NINE patients with recurrent affective disorders were examined for previous suicide attempts. Twenty-six patients with previous suicide attempts were compared to 73 patients with no previous attempts on a variety of study variables. Suicide attempters had an earlier age of affective illness onset and were more likely to have a past history of alcohol abuse. The possibility that these findings may be related to serotonin abnormalities is discussed.

Death by suicide in the United States is estimated to occur at a rate of approximately 40 per 100,000 per year in adult males and 10 to 15 per 100,000 in adult females.[1-3] This suggests that at least 35,000 adults die by suicide each year. The actual number of suicide deaths is probably much greater.[4]

Successful suicides are associated with psychiatric illnesses, especially affective disorders.[5-10] Several studies suggest that the overall incidence of completed suicide in manic-depressive disease may be as high as 15 percent.[10-15] Alcoholic intoxication has a strong association with both completed and attempted suicide.[16-18]

Contrary to some popular notions, completed suicides are associated with previous suicide attempts.[9,19-22] However, most suicide attempters do not complete suicide.[22-24] Seriousness of previous suicide attempts correlates positively with completed suicide.[22] The feeling of hopelessness is associated with the medical and psychiatric seriousness of a suicide attempt.[25-26]

During the past decade a variety of research suggests that many psychiatric symptoms could likely be the result of specific neurophysiological malfunctions (e.g., neurotransmitters imbalances). Although the data are inconclusive, there is the suggestion that abnormalities of serotonin metabolism may be involved in suicidal behavior. A review of the literature involving serotonin metabolism and suicides has recently been presented.[27]

The hypothesis that specific neurotransmitter abnormalities may underlie suicidal behavior suggests that suicidal patients could have certain features of their affective disorder in common when compared to nonsuicidal patients. This study examines this hypothesis by comparing a relatively homogeneous group of affectively disordered patients who have made previous suicide attempts to a group with no history of suicide attempts.

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METHODS

Study patients were all participants of a long-term study of affective disorder prophylaxis. Selection criteria applied to consecutive affectively disordered inpatients and outpatients included: (1) diagnosis of either major depressive disorder or manic disorder (research diagnostic criteria—RDC), (2) age 18 to 65, (3) at least two distinct affective episodes (including the index episode) during the past 30 mo, and (4) no recent history of a major nonaffective psychiatric disorder. Patients meeting study criteria were given a structured interview during the following week. This interview included the schedule for affective disorders and schizophrenia—life—time version (SADS-L).

Patients were considered to have made a suicide attempt if they had previously undertaken a self-destructive act with the thought of killing themselves. Suicide attempters were questioned about the number of previous attempts and the specifics of their most serious attempt.

Study variables that were examined included sex, patient age, affective polarity, current symptomatology, duration of current episode, number of affective episodes, age of first affective episode, marital status, work history during the past 5 yr, history of prior outpatient treatment, history of previous psychiatric hospitalizations, total time hospitalized during past 5 yr, longest major depressive episode, best level of social relations during past 5 yr, quality of remissions (i.e., level of interepisode functioning) during past 5 yr, length of most recent remission, and family history.

Chi-square analyses were performed on categorical variables and analyses of variance were used for continuous variables. Two-tailed t tests were used.

RESULTS

Three hundred affectively disordered patients were interviewed for study participation. Of these, 105 patients met selection criteria. Information about suicide attempts was available for 99 patients (74 females and 25 males). Forty-eight patients were bipolar and 51 were unipolar. Twenty-six patients had attempted suicide previously and 73 had not.

Table 1 lists study variables that were statistically significant at the $p < 0.01$ level. Those variables reaching a level of significance ($0.01 < p < 0.05$) may best be considered as showing a trend, in view of the number of variables tested and the fact that some of the variables were related to one another. Trends were found for suicide attempters spending more total time hospitalized ($p < 0.02$) and experiencing poorer interepisode functioning ($p < 0.05$).

No significant differences were found between groups with respect to sex, affective polarity, duration of affective episodes, number of affective episodes, 5-year work history, total number of hospitalizations, age of first hospitalization, duration of longest affective episode, having ever experienced a psychotic depression, or family history for affective disorders. RDC subtype diagnosis at

Table 1. Comparison of Suicide Attempters to Nonattempters

	Nonattempters	Attempters	*p*
	n = 73	*n* = 26	
Age of first affective episode (mean)	29 ± 13	21 ± 6	0.001
Age at index interview (mean)	39 ± 14	32 ± 9	0.01
Ever diagnosed alcohol abuse (RDC)	9 (12%)	12 (46%)	0.0008
Global assessment scale (index episode)	48 ± 8	41 ± 10	0.001

index interview, duration of most recent remission, individual depressive symptoms, or index interview Hamilton or Raskin depression scores likewise showed no significant differences between groups.

Fifteen (or 58%) of the suicide attempters had more than one attempt, with eight attempts representing the largest number of previous attempts. The number of suicide attempts was positively correlated with the medical seriousness of the patient's most serious attempt (Pearson correlation coefficient 0.56; $p < 0.001$).

DISCUSSION

Results of this investigation suggest that affectively disordered patients who have made previous suicide attempts differ from patients who have not attempted suicide. Suicide attempters had an earlier age of illness onset and were more likely to have been diagnosed alcoholic in the past. There was also a trend for suicide attempters to have experienced poorer interepisode functioning and to have spent more time hospitalized.

The associations reported in Table 1 between suicidal behavior and past history of alcohol abuse, and earlier age of illness onset, may be explained by low levels of brain serotonin. Previous research examining the relationship of suicide to brain levels of serotonin and its metabolite 5-hydroxyindoleacetic acid (5HIAA) has produced conflicting results.[27] Methodological problems including sample selection and assaying procedures may account for some of the contradictions. A recent prospective study of depressives and suicide attempters revealed violent suicide attempts and completed suicides were associated with low cerebrospinal fluid (CSF) levels of 5HIAA.[28]

Studies of the relationship of alcoholism ot 5HIAA levels have produced discrepant results.[29-32] Selection of sampling times may explain some of the differing results. Examination of alcoholics during intoxication and for several days thereafter has revealed normal, decreased, or increased levels of 5HIAA.[29-32] Three studies examining abstinent alcoholics all reported lowered CSF 5HIAA levels.[30-32]

The low levels of 5HIAA reported in abstinent alcoholics is consistent with the hypothesis that low levels of brain serotonin may play an etiologic role in some forms of alcoholism.[32] The reported serotonin deficiency in alcoholism and suicide, although not conclusive, is consistent with the association we found between attempting suicide and past history of alcohol abuse ($p < 0.0008$).

Interestingly, depressives with a positive family history of alcoholism were found to have significantly lower CSF 5HIAA than did depressives with a negative family history of alcoholism.[33] This could indicate that low serotonin levels underlie depressive illness and alcoholism in some families.

The relationship of age of onset of affective disorders to serotonin levels has not been adequately examined. One study reported depressives with low CSF 5HIAA to be significantly younger at index interview (33 versus 59; $p < 0.001$) than patients with high or normal 5HIAA.[34] This suggests the possibility of an earlier age of onset in the low 5HIAA group. If true, it would be consistent with our finding of an association between suicide attempts and earlier age of illness onset, both of which may be related to low serotonin levels. Another investiga-

tion, however, reported no difference in age of onset between a group of depressives with low CSF 5HIAA and depressives with normal or high 5HIAA.[33]

Many depressed patients with low levels of 5HIAA during a depression experience no change in 5HIAA when depressive symptoms improve.[35,36] It is possible that this subgroup of depressives has a remission of most or all their depressive symptomatology but continues to experience more subtle difficulties in their functioning secondary to subnormal serotonin metabolism. This could serve as an explanation for our observation of mild interepisode dysfunction in the group of suicide attempters. A previous investigation reported a significant relationship between the SADS-L item of social isolation and previous suicide attempts.[37]

The positive correlation found between the number of suicide attempts and medical morbidity of the most serious suicide attempt contrasts with the commonly held belief that patients making frequent atempts are not serious about suicide. This association of medical seriousness of an attempt with a large number of attempts may not be true for nonaffectively disordered suicide attempters.

The notion that a single neurotransmitter (i.e., serotonin) could be responsible for suicidal behavior and the associated findings reported in Table 1 may prove to be an oversimplification. Future research may be able to clarify if serotonin abnormalities underlie such seemingly diverse depressive features as age of onset, abuse of alcohol, and suicidal behavior.

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