Is There a Tardive Dysmentia?


Abstract

A change in the phenomenology of schizophrenia has been observed over the past several decades; affective disturbances and phasic courses have become more evident. Although there is no obvious single explanation for these changes, several ideas have been considered. The advent and use of antipsychotic drugs over the past 30 years stands out as the most significant change. Because it is well known that chronic treatment with antipsychotic drugs can induce tardive dyskinesia and has been hypothesized to induce a supersensitivity psychosis, it is reasonable to believe that other behavioral changes may occur over time. We here describe a behavioral disorder that we have termed tardive dysmentia, involving changes in affect, activation level, and interpersonal interaction. A relationship between tardive dysmentia and tardive dyskinesia is suggested. It is our hypothesis that tardive dysmentia contributes to the changing course of schizophrenia and occurs after long-term treatment with antipsychotic drugs.

Schizophrenia and its treatment have changed over the same epoch of time. The change in the illness has been noted by several authors and was the focus of an earlier issue of the Schizophrenia Bulletin (Vol. 3, No. 4, 1977). Observations of change have been made by both European and American psychiatrists and may be exemplified by the comments of experienced clinicians. Bleuler (1973) concluded:

The most severe psychotic conditions are milder than before; the chronicity of schizophrenic psychosis (in particular chronic hospitalization in schizophrenia) has become less frequent, while phasic course (hospital discharges and readmissions) has become more frequent. [p. 73]

Romano (1977) similarly stated:

Schizophrenic illnesses today are milder and . . . one rarely sees patients experiencing an unremitting catastrophic course. Hebephrenic and catatonic subtypes occur less often, but some of this behavior may be included in the designated subtypes of acute and chronic undifferentiated schizophrenia. One sees more patients with phasic psychotic episodes with greater affective components. [p. 555]

In his review of the literature Hogarty (1977) reminded us of the pitfalls in determining whether schizophrenia has changed when the validity of the diagnostic process is uncertain. Nevertheless, his assessment of the literature was as follows:

The evidence, as confounding as it might be, suggests that the change has been for the better, with a decline in the more typical schizophrenic symptoms, but with a corresponding increase in milder deficits, particularly those of an affective nature. [p. 595]

These observations are compatible with the dramatic increase in the number of relapses and the readmissions of schizophrenics to psychiatric facilities in the last 20 years reported by Taube (1974). Although there is general agreement that this change has occurred, there is no consensus about its cause.

What are the factors that could mediate the change? Hare (1974) has pointed out that there is an inevitable mutability in disease so that the course of schizophrenia may have changed because of evolution of the disease process in response to cul-

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Tardive dyskinesia has emerged as a chronic problem for schizophrenic patients over time. This condition represents a disturbance in brain function and is of particular relevance to the hypothesis of tardive dyskinesia. The behavioral changes observed in chronic schizophrenic subjects with severe tardive dyskinesia presented with behavior resembling that of hypomania as well as schizophrenia. The patients tended to be loquacious and to speak in a loud voice. They showed thought disconnection and were generally circumstantial and aimless in conversation. Disassociated, inappropriate statements were common. The prevailing mood was generally one of euphoria, but unheralded, inexplicable, explosive changes in affect occurred as good humor changed rapidly to explosive hostility or sullen petulance. Social withdrawal and autistic preoccupation were punctuated by episodes of overactive behavior when the subject spoke loudly, often close to the observer's face, and was quite intrusive and invasive of the privacy of others. The early interpretation of this phenomenon was that these patients had been initially misdiagnosed as schizophrenic but were actually manic-depressive or schizoaffective. However, in referring to their clinical records, it was noted that most of these subjects had presented originally with characteristic schizophrenic features including formal thought disorder, autistic preoccupation, auditory hallucinations, flattening of affect, anergia, and social withdrawal. The initial psychiatric diagnosis appeared to have been accurate. It was then hypothesized that the current clinical picture was in fact a combination of ongoing schizophrenic pathology and behavior deriving from neuroleptic-induced brain changes. The inference was that the pathophysiological mechanisms responsible for the drug-induced behavioral changes were similar to those leading to tardive dyskinesia. Therefore, it was reasoned that a correlation should be present between the behavioral disorder and tardive dyskinesia.

Methods

Twenty-nine patients (16 males, 13 females), ages 48.8 ± 12 years (mean ± SEM), range 23–74 years, were chosen from a continuing care ward of Dorothea Dix Hospital to participate in the study. Selection criteria included at least 2 years of continuous neuroleptic therapy. In fact, all patients considerably exceeded this minimum with the mean months on neuroleptics being 204 ± 87, range 48–300, and the mean total months of hospitalization 202 ± 107, range 60–384. DSM-III diagnoses included 27 patients with chronic undifferentiated schizophrenia, 1 patient with chronic paranoid schizophrenia, and 1 patient with bipolar disorder, manic.

Interviews with the patients were performed by two of us (I.C.W. and J.C.G.) and generally lasted 45 minutes. During the interview one of us talked with the patient while the other observed. The interview was designed to ascertain two characteristics: presence of tardive dyskinesia and emotional behavior. Each patient was engaged in an open-ended discussion of why he/she was in the hospital and how he/she felt currently. Dyskinesia was rated on the Abnormal Involuntary Movement Scale (AIMS) (1976) following the standard format. Stereotypies and mannerisms were differentiated from dyskinesia. Emotional behavior was rated on five 100 mm line tests designed for their relevance to the hypothesized tardive
dysmentia. The scoring continua on the individual line test were as follows: (1) from depressed mood to euphoria; (2) from stable mood to labile mood; (3) from quiet speech to loud speech; (4) from paucity of words to excess of words; (5) from retreat from the examiner to approach to the examiner. The 100 mm line test has previously been shown to be an accurate and reliable measurement of behavior (Zealley and Aitken 1969). All scales were completed independently by both examiners immediately after the interview. Interrater reliability, determined by Spearman rank coefficient of correlation, was as follows: AIMS, .887 (p < .01); euphoria, .869 (p < .01); unstable mood, .335 (p < .05); loud speech, .896 (p < .01); excessive words, .734 (p < .01); approach to examiner, .621 (p < .01). The Spearman rank coefficient of correlation between individual line tests using the mean scores between raters is shown in Table 1. Positive relationships occurred between all variables, reaching statistical significance in all but one instance.

**Results**

The distribution of the AIMS scores is shown in Figure 1. Three of the hypothesized tardive dysmentia behaviors—unstable mood, loud speech, and approach to the examiner—were significantly correlated with the total AIMS score (Table 2). Although age was not significantly correlated with the AIMS score (r = .28), we used the partial Kendall correlation to control for age. When this was done, loud speech and unstable mood were significantly correlated with the AIMS score (Table 2). Furthermore, positive correlations were present between months on neuroleptics and the mean AIMS score (r = .31) and between months on neuroleptics and three of the measures of tardive dysmentia: unstable mood (r = .32), loud speech (r = .23), and euphoria (r = .20).

**Discussion**

This study showed positive relationships between the severity of tardive dyskinesia and the predefined tests for what we have termed tardive dysmentia. These findings suggest that

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†p < .01.
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characteristic changes in emotion and behavior are associated with tardive dyskinesia in some chronically ill patients. One interpretation of these results is that long-term neuroleptic therapy may result in alterations to areas of the central nervous system concerned with the expression of emotion and thought. Other plausible explanations are that the level of anxiety, psychosis, or affective state or recent changes in antipsychotic medication may have contributed to an exacerbation of tardive dyskinesia and the tardive dysmentia behaviors. Although we do not have behavioral ratings of anxiety or psychosis taken at the time of the interview, it is our clinical impression that the patients with tardive dysmentia behaviors were neither more anxious nor more psychotic than the patients without the dysmentia behaviors. In fact, patients with dysmentia actually appeared more at ease with the interviewers. Similarly, as regards psychosis, patients with tardive dysmentia did not seem more psychotic in the sense of greater delusional ideation, hallucinations, or formal thought disorder. Affective changes have recently been noted to play some role in the expression of tardive dyskinesia; in particular, switches into depression may worsen tardive dyskinesia (Cutler et al. 1981). However, we did not find a significant correlation between the line test measuring depressed mood to euphoria and the AIMS score. Therefore, although we cannot eliminate affective change as contributing to the dyskinesia and the dysmentia, it seems unlikely that this was a major factor. Furthermore, the observations of Cutler et al. (1981) were made on two patients with manic-depressive illness whereas our patients were schizophrenic and the observation was that depression not euphoria aggravated tardive dyskinesia. The question of medication change is an important one, but in almost all cases the patients were maintained on stable doses of antipsychotic drugs and had been for some time.

Methodological problems notwithstanding, is there any theoretical basis which would make plausible behavioral consequences from long-term neuroleptic administration? The best studied phenomenon in this regard is, of course, tardive dyskinesia. The current hypothesis of the pathophysiology of tardive dyskinesia is that subchronic or chronic administration of neuroleptics leads to hyperactivity of the dopaminergic nigrostriatal pathway. The underlying mechanism has not been found, though an increase in striatal post-synaptic dopamine (DA) receptors accompanied by a supersensitive response to apomorphine has been observed in animals after chronic neuroleptic administration (Tarsy and Balldessarini 1974). The idea that similar changes may occur in other brain regions is not new; Davis and Rosenberg (1978), Chouinard and Jones (1980), and Ungerstedt and Ljungberg (1977) have discussed the possibility of a DA supersensitivity psychosis. Clinically this is supported by the data of Chouinard and Jones (1980), who reported a subpopulation of schizophrenic patients who require increasing and high dosages of fluphenazine for symptom control, relapse rapidly on drug withdrawal, and exhibit a high incidence of tardive dyskinesia. Furthermore, increased binding of \(^3\)H-haloperidol and \(^3\)H-sparperone has been reported in the nucleus accumbens, a projection field of the mesolimbic DA system, of schizophrenic patients treated with neuroleptics (Lee and Seeman 1980). This suggests proliferation of DA receptors with resulting increased DA transmission. In animal models chronic neuroleptic administration has been reported to increase locomotor response to a DA agonist injected into the nucleus accumbens (Davis, Hollister, and Fritz 1978) and to increase \(^3\)H-haloperidol binding (Muller and Seeman 1977). These findings taken together suggest that chronic neuroleptic administration may induce behavioral alterations in man quite apart from similar and traditionally recognized changes in motor function. Thus it may be that neuroleptic-induced changes in limbic or cortical DA pathways produce a complex behavioral syndrome, which we have identified as tardive dysmentia.

As noted, a prominent theme in the current psychiatric literature is...
that changes are occurring in the clinical course of schizophrenia. Many theories have been advanced to account for this based on social, psychological, psychotherapeutic, and pharmacotherapeutic factors (Schooler 1976; Vaughn and Leff 1976; Murphy 1977; Tissot 1977). We postulate, without discounting the importance of other variables, that the changing natural history of schizophrenia is to an important extent dependent on the neurotoxic effects of chronic neuroleptic medication. Greater attention is also being given to the increased incidence of the clinical features of affective disorder in the chronic schizophrenic population (Freedman 1979). A widespread interpretation of this phenomenon is that these patients were initially manic-depressive patients misdiagnosed as schizophrenics. However, a review of the clinical histories of our study population showed that in a preponderance of subjects the initial diagnosis of schizophrenia was unequivocal. Studying the records over the years, we noted that the intrusion of symptoms of affective disorder was gradual and insidious until eventually the clinical description was more appropriate to a mani-depressive or schizoaffective diagnosis. The unwary clinician is then "set up" to diagnose this pseudo-manic-depressive disease as a "true" manic-depressive illness.

Our study was based on a single clinical interview. However, it has been our clinical experience that the symptoms of tardive dyskinesia and tardive dysmetria show positive covariance over time. We would be interested to know whether other clinicians have observed what we have termed tardive dysmetria.

References


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Announcement

The 12th Annual Newer Strategies Series Symposium, sponsored by the Joint Committee on Schizophrenia of the New York State Psychiatric Association, will be held this fall in New York City.

The theme, date, and presenters are not available at the present time. Those wishing to be placed on the mailing list for this information should address their requests to:

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