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The Prevalence of Presumed Tardive Dyskinesia in Psychiatric Inpatients and Outpatients

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Abstract. Randomly selected psychiatric patients (271 total) were examined by raters blind to diagnosis and treatment history for the presence of abnormal movements. The prevalence of presumed tardive dyskinesia among neuroleptic-exposed patients was 4.6%. If minimal rating scale criteria were applied, 9% of those patients with no history of neuroleptic exposure might have been given 'presumptive' diagnoses of dyskinesia. Problems in establishing diagnostic criteria are discussed and a longitudinal approach toward validating diagnoses is recommended.

Key words: Tardive dyskinesia – Abnormal involuntary movements – Neuroleptic side effects

The syndrome referred to as tardive dyskinesia (TD) has been recognized since the late 1950's (Schönecker, 1957). Increasing concern about this condition has led to numerous investigations of 'prevalence' and 'risk factors'. Considerable confusion has arisen due to the enormous range of prevalence estimates found by different investigators at different institutions (Baldessarini and Tarsy, 1978). No doubt much of this variance is due to real differences in patient populations. However, it appears likely that an additional factor is the lack of validated operational criteria which can be used to make a diagnosis.

Prevalence surveys have generally involved the rating of abnormal involuntary movements on scales designed to assess or measure such movements. Gardos et al. (1977) have critically reviewed the variety of assessment techniques currently being applied to TD and pointed out the potential deficiencies of each.

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Given the limitations of current techniques for assessing dyskinesias, it is even more problematic to employ rating scales to make a diagnosis, a function for which they are generally not intended. Diagnosis in medicine, and particularly psychiatry, should be a process which involves far more than scores on a rating scale, though such scores may be useful for screening purposes to suggest further investigation.

Despite these caveats, the prevalence surveys have served a heuristic function of sorts. At the same time, however, the potential harm of overdiagnosis in a complex area, with major public health, legal, and ethical implications must be considered.

This investigation was designed to determine the prevalence of presumed TD in our patient population and, at the same time, to determine the prevalence of possible false positives using raters blind to the patient's diagnosis and drug history who would make a presumed diagnosis based on one examination.

Materials and Methods

A random sample of 120 Hillside Division inpatients and 151 outpatients attending our aftercare clinic were examined (after giving consent) by two raters simultaneously using a systematic examination format for TD. This format combines procedures outlined in the Abnormal Involuntary Movement Scale (AIMS) (Guy, 1976) and instructions designed for the Simpson Dyskinesia Scale (SDS) (Simpson, 1979). Each patient was examined for a minimum of 10 min. The examination included removal of shoes and socks and several 'recruitment' or 'activation' procedures. The same procedures were used in examining each patient. Both raters were blind to the patient's diagnosis and medication history, and rated independently. The SDS was used to rate specific movements. In addition to these measures, a 6-point global rating scale was employed: Absent (0); questionable (1); mild (2); moderate (3); moderately severe (4); and severe (5). Raters had undergone extensive training involving both live examinations and rating of videotapes. The κ statistic, a reliability measure used with nominal scale data (Cohen, 1960; Bartko and Carpenter, 1976), showed that interrater agreement for global judgments was adequate (unweighted $\kappa = 0.7068 \pm 11$; $Z = 6.425$, $P < 0.001$).

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Table 1. Characteristics of the study population ($N = 271$)

Exposure to neuroleptics	
Never	11.8%
Currently receiving	56.8%
Within past year	17.7%
Not within past year	13.7%
Diagnoses	
Schizophrenic (all subtypes)	53.9%
Manic depressive (all subtypes)	20.6%
Organic brain syndrome	2.6%
Minor depressive disorder and personality disorders	22.9%

Table 2. Characteristics of patients exposed to neuroleptics ($N = 239$)

Predominant type of neuroleptic received during treatment	
Aliphatic	23.4%
Piperazine	44.3%
Piperidine	16.3%
Butyrophenone	8.4%
Thioxanthene	3.8%
Dihydroindolone	0.4%
Dibenzoxazepine	1.7%
Indeterminate	1.7%
Maximum neuroleptic dosage received for minimum of 1 month (in chlorpromazine equivalents)	
25 – 500	38.5%
500 – 1,000	26.3%
1,000 – 1,500	13.4%
1,500 – 2,000	7.1%
2,000 – 2,500	2.9%
2,500 – 3,000	2.1%
3,000	3.8%
Indeterminate	5.9%

The demographic characteristics of the patients are presented in Table 1. The mean age of the sample was 31.8 ± 13.5 years. There were 132 males (48.7%) and 139 females (51.3%). The most frequent diagnosis was schizophrenia of varying subtypes (53.9%).

Fortunately, for the purposes of this study, 32 patients (11.8%) had no history of exposure to neuroleptics. Of those patients exposed to neuroleptics, duration of drug treatment was 3 months or less for 23.4%, 3 – 6 months for 7.5%, 6 – 12 months for 15.1%, 1 – 2 years for 18.8%, 2 – 3 years for 13%, and drug treatment for more than 3 years was seen in 20.1% (in 2.1% it was impossible to tell). Among the neuroleptic-exposed group, 15% had not been exposed within the past year.

Since there are no definitely established criteria for determining TD, accurate diagnosis remains a serious problem. A certain number of abnormal movements are seen among one's colleagues or 'normal controls', therefore, it was important to have a global rating which acknowledges the possibility that observable movements can occur which may not be pathological. Unfortunately, the global severity item on the AIMS does not allow for this distinction, whereas the area items do.

The global item added to the SDS was intended to allow for 'questionable' cases. The real meaning of this categorization can only be determined by prospective studies; i.e., do they eventually evolve into more definite cases or is this a potentially benign finding?

Realizing that it is somewhat premature and arbitary to define a threshold for TD (and obviously prevalence will diminish as thresholds are made more conservative), for the purposes of this survey it was decided, a priori, that both raters had to agree on a global rating of at least 2 (mild) to consider abnormal involuntary movements to be present. In addition, videotapes were made whenever possible to be reviewed by others for confirmation. In effect, these ratings were used as a screening device to identify individuals requiring further diagnostic work for abnormal involuntary movements.

Results

Of the 271 patients examined, 11 received global ratings of at least 2 from both raters, a prevalence of 4%. However, since 32 patients had no history of exposure to neuroleptics, the prevalence among neuroleptic-exposed individuals was 4.6%. If one includes any questionable rating by either examiner the prevalence in the total sample increased to 22.2%, but also included three patients with no history of exposure to neuroleptics who might, therefore, be considered false positives. Two of these three patients received ratings of ≥ 1 from both raters, which we feel supports the value of the questionable category in reducing false positives. One of the patients received a diagnosis of presumed Huntington's chorea based on family history (Table 3). The prevalence of any rating of questionable or more among neuroleptic-exposed patients was 21%.

Analysis of Risk Variables. The global score for the two raters were summed and the relationship of these scores to a variety of risk variables was assessed. Among those patients exposed to neuroleptics, one set of correlations was carried out using a dichotomous classification for dyskinesia, any positive global score ($N = 50$) versus global scores of zero ($N = 189$). A second set of analyses was carried out dividing the sample into 'definite' cases (those who received global ratings of ≥ 2 from both raters) versus all others (Table 4).

In the first analysis, significant positive correlations were found between dyskinetic signs (questionable or definite) and the following variables: Age; duration of exposure; potency of neuroleptics; maximum neuroleptic dose received; history of electroconvulsive therapy (ECT); and number of ECT treatments. When the analysis separated those with definite signs, only high potency neuroleptics remained significantly correlated. There were no significant differences between inpatients and outpatients either with regard to prevalence of positive ratings or risk factors.

Given the fact that only 11 cases were included in the definite group, any statistical analysis is made problematic. The types of statistical analysis necessary to sort out potentially meaningful relationships (e.g., discriminant function analysis or multiple regression techniques) are not suitable for the numbers we are

Table 3. Cumulative frequencies and proportions of positive ratings by neuroleptic exposure

	Summed global criterion (two raters)				
	0	≥1	≥2	≥3	≥4
Neuroleptic exposure (N = 239)	189 (79%)	50 (21%)	33 (14%)	14 (6%)	11 (5%)
No neuroleptic exposure (N = 32)	29 (91%)	3 (9%)	2 (6%)	2 (6%)	1 (3%)

Table 4. Variables related to presence of abnormal involuntary movements at different criterion levels among patients exposed to neuroleptics (N = 239)

Variable	Two raters (summed global, ≥1 versus <1)			Two raters (both global, ≥2 versus others)		
	r	N	P	r	N	P
Sex	0.06	239	NS	0.07	239	NS
Age	0.15	239	0.02	0.02	239	NS
Duration of exposure	0.15	235	0.03	0.05	235	NS
Potency	0.17	236	0.007	0.14	236	0.03
Maximum dose (1 month, chlorpromazine equivalent)	0.17	226	0.01	0.04	226	NS
Duration of AP (Antiparkinsonian) exposure	0.03	236	NS	0.03	236	NS
ECT[a]	0.16	239	0.01	0.07	239	NS
Number of ECT	0.12	239	0.06	0.03	239	NS
OBS (Organic brain syndrome)	0.05	239	NS	0.08	239	NS

[a] Electroconvulsive therapy

Table 5. Simpson scale items in questionable cases of tardive dyskinesia (N = 39)

Simpson item[a]	Patients with sign present[b]	Percent of questionable sample %
Choreoathetoid movements of the tongue	34	87
Tremor of eyelids	24	62
Tongue tremor	22	56
Chewing movements	18	46
Choreoathetoid movements of the fingers	14	36
Puckering of lips	8	21
Tic movements	8	21
Blinking of eyes	7	18
Smacking of lips	6	15
Clamping movements while sitting	5	13

[a] Only items on which at least five patients showed the sign are listed
[b] Seen by either rater and rated at least a 1 on the Simpson scale

dealing with. Since we are all eager to identify important risk variables, there has been a tendency to perform rather dramatic statistical overkill on limited data. There are also inherent risks in doing multiple correlations in a single sample where some significant correlations may be found by chance.

The questionable group included 39 patients. As can be seen in Table 5, the most frequently observed signs were choreoathetoid movements of the tongue, tremor of eyelids, tongue tremor, chewing movements, and choreoathetoid movements of the fingers. It has been our impression that choreoathetoid movements of the tongue are a particularly important sign of TD, and 86% of the questionable cases displayed some suggestion of this.

The three cases of false positive patients are considered unusual, and a brief clinical note describing them appears warranted.

Case 1. Patient was a 69-year old psychotically depressed white male, whose first psychiatric hospitalization was at age 35 for depression and a suicide attempt. He was treated with ECT with good response, and functioned well for the next 34 years. The chief complaints of this hospitalization included depression, insomnia, weight loss, anhedonia and suicidal ideation. He was placed on amitriptyline (50–200 mg) for 1 month prior to examination, and was receiving 200 mg on the day of rating. His response to antidepressant medication had been poor. Psychological testing suggested organic

impairment. The TD examination revealed mild tremor of eyelids and mild choreoathetoid movements of the tongue. Global TD ratings were 1 (questionable) and 0 (absent).

Case 2. Patient was a 34-year old obese white female, hospitalized for the first time, with complaints of compulsive eating, phobic behavior, and depression. Neurological examination was within normal limits, but psychological testing suggested organic impairment. The TD examination revealed questionable smacking and chewing movements, questionable tongue protrusion, and mild choreoathetoid movements of the tongue. Global TD ratings were 1 (questionable) and 2 (mild).

Case 3. This was the first hospitalization for this 30-year old white female diagnosed as mixed character disorder with complaints of depression and a fear of losing control. On examination she showed an unsteady gait with uncoordinated hand and foot movements. The patients' paternal grandmother had Huntington's chorea. Her father also had a history of unsteady gait, but had never been diagnosed. Neurological consultants suspected that she had Huntington's Chorea. In addition, psychological testing indicated some organic impairment. The TD examination revealed mild choreoathetoid movements of the tongue and fingers, as well as mild to moderate tic movements and mild carressing of face and hair. Global TD ratings were 1 (questionable) and 3 (moderate).

In case 1, the patient was receiving amitriptyline, a drug with anticholinergic properties. Hypocholinergic functioning has been implicated in the pathophysiology of TD (Gerlach et al., 1974) and cases of dyskinetic movements attributed to tricyclic antidepressants have been reported (Fann et al., 1976).

Of interest is the finding of cognitive impairment in the psychological test results of all three patients. In case 3, the impairment is probably a sequela of the disease process.

Prospective Assessment. Our current approach to the diagnosis of TD is a longitudinal rather than a cross-sectional one. We believe that this approach is necessary in establishing the validity of the diagnosis. In keeping with this, we have attempted to follow up on those patients who received a diagnosis of presumed TD in this prevalence survey. We were able to re-examine 10 of 11 patients at intervals from 2 months to 1 year. All of these patients continued to manifest dyskinetic signs and symptoms consistent with the diagnosis of TD. The intervening clinical treatment of these patients varied, as one would expect: Some were successfully withdrawn from neuroleptics, while others relapsed following drug withdrawal and received a further course of neuroleptics. The equally important question as to the outcome of those patients with questionable signs is currently the subject of a long-term, large scale prospective study at our institution.

Although no follow-up data are available on these questionable cases, preliminary data from our prospective study suggest that patients with questionable signs of TD have a three fold greater chance of developing TD than nonquestionable patients over a 6-month period. Moreover, of the 20 patients who developed TD during the course of our prospective study, 14 (70%) had been rated as questionable cases preceeding the TD diagnosis (Kane et al., 1979). We also feel that the roles of various putative risk factors are best assessed in prospective studies since reliable retrospective data are difficult to obtain.

Discussion

We have found a 4.6% prevalence of TD among a sample of 239 patients exposed to neuroleptics. This prevalence rate is considerably lower than many appearing in the literature. We feel this may in large part be due to the relatively young age of our population and their relatively shorter exposure to neuroleptics than many chronic-state inpatients frequently included in prevalence estimates. It is also likely that if all patients receiving neuroleptics had their medication discontinued an additional number of socalled 'latent' or 'covert' dyskinesias would be detected. However, we feel that diagnostic criteria remain a potentially significant variable. Our blind examination of 32 patients with no history of neuroleptic exposure revealed three cases (9%) who might have been given a diagnosis of TD based on minimal rating scale criteria, if drug histories were ignored.

Perhaps our threshold for making a presumed diagnosis is more conservative than other investigators, and this would likely increase false negative diagnoses as it reduces false positives. The fact that some significant (though weak) correlations were found between putative risk factors and questionable ratings might suggest that these ratings are discerning a drug effect. In addition, prospective data suggest that questionable signs may indicate increased risk for development of more clear-cut TD.

We are not suggesting that our utilization of one examination and its resulting scores on a rating scale is an improvement of previous attempts. We feel the data presented should discourage us from making diagnoses based on rating scale scores, and such a strategy is useful as a screening devise. We urge caution in the diagnosis of TD, a diagnosis which carries with it significant potential ramifications, and recommend a

longitudinal approach which should be helpful in establishing diagnostic validity.

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