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WB: rating scales increase prevalence by factor of almost 3

An Assessment of Tardive Dyskinesia in Schizophrenic Outpatients

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Abstract. An examination of tardive dyskinesia in 213 schizophrenic outpatients using the Abnormal Involuntary Movement Scale (AIMS) indicates that increasing age is significantly associated with the presence of this disorder while sex is not. Both sexes showed significant linear increases with increasing age. Although males did not evidence the statistically significant curvilinear trend previously reported in an inpatient study using the same methodology, they displayed an attenuated effect at the older age levels. A comparison of prevalence values between the outpatient sample and the inpatient sample previously studied indicated no greater prevalence in the outpatients. However, an examination of differences in AIMS total scores between these samples suggested the presence of many more marginal and mild movements in the outpatients. Reasons for the differences between the inpatient and outpatient studies are discussed.

Key words: Tardive dyskinesia – Movement disorders – Neuroleptics – Extrapyramidal system – Side effects

In recent years numerous estimates of the prevalence of tardive dyskinesia have been reported. Kazamatsuri et al. (1972) in a review of 23 studies found prevalence estimates varying 0.5 – 41.3%. The discrepancies among the results of these studies are probably due to a number of factors including the type of assessment technique employed and the demographic and treatment characteristics of the sample tested. A variety of methods have been used to obtain prevalence estimates of tardive dyskinesia including questionnaires to ward physicians, global clinical judgements, and detailed rating scales. A review of 15 of 17 English language studies cited in the review by Kazamatsuri et al. (1972) revealed that those which used at least an ordinal rating scale (Pryce and Edwards, 1966; Siede and Müller, 1967; Crane, 1968a, b; Edwards, 1970; Dynes, 1970; Kennedy et al., 1971; Brandon et al., 1971) reported an average prevalence nearly three times greater than those which used questionnaires or global clinical judgements (Hunter et al., 1964; Faurbye et al., 1964; Demars, 1966; Dincmen, 1966; Crane and Paulson, 1967; Turunen and Achté, 1967; Ettinger and Curran, 1970).

In addition to the method employed, the criterion level of symptomatology used to define the disorder will influence prevalence estimates. Inclusion of questionable or mild movements in the definition of tardive dyskinesia has been shown to inflate prevalence estimates while use of a criterion based on the prevalence of only severe symptomatology will lead to gross underestimation (Smith et al., in press). Choice of a criterion also appears to affect differences in prevalence between the sexes (Smith et al., 1979). The more severe the criterion, the more likely it is that one will find a greater prevalence of the disorder in females.

Finally, characteristics of the patient population can affect prevalence estimates. Smith et al. (1978) rated 293 schizophrenic inpatients on the Abnormal Involuntary Movement Scale (AIMS) and found significant age and sex interactions for dyskinetic symptomatology. In females the amount of dyskinesia was found to increase linearly with increasing age while in males there was a significant curvilinear relationship. Females displayed twice the prevalence of dyskinetic symptomatology only for the two oldest age groups (70 – 79 and ≥ 80 years). Thus, the age and sex characteristics of the sample studied can influence the results of any prevalence study and failure to include both sexes and patients at various ages across the life span will

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undoubtedly lead to confusion and misleading results. Furthermore, since it is possible that the high levels of dyskinesia in inpatients might reflect a tendency of organically involved or nondrug responding patients to accumulate in an inpatient setting, studies in outpatients are necessary to obtain complete prevalence estimates. To date there have been few published studies of tardive dyskinesia in outpatients. Asnis et al. (1977) have recently reported the results of a survey of 69 neuroleptic-treated outpatients. Thirty patients (43.4%) were diagnosed as having tardive dyskinesia. This finding is particularly disturbing when the characteristics of their sample are considered. The mean age of the study group was 45.5 years and of those diagnosed as dyskinetic 46.7% had a duration of neuroleptic treatment of 2 years or less.

The present study was conducted to determine whether the previously reported age and sex trends in dyskinesia were also present in schizophrenic outpatients and to assess the prevalence of tardive dyskinesia in this sample using the same methodology employed in a previous inpatient study of this disorder (Smith et al., 1978, 1979).

Materials and Methods

Subjects. All patients attending six day-center facilities and one group home and having a primary or secondary diagnosis of schizophrenia were asked to participate in the study. The sample was restricted to those attending a day-center type of setting because one of the scales (NOSIE-30) required staff to be familiar with a patient's daily behavior.

A total of 213 outpatients participated with a mean age of 54.6 years and a mean of 24.8 years since first hospitalization. Males ($N = 96$) had a mean age of 52.8 years (SD = 18.58) with a mean of 24.2 years (SD = 16.04) since first hospitalization. Females ($N = 117$) had a mean age of 56.1 years (SD = 15.71) with a mean of 25.2 years (SD = 13.71) since first hospitalization.

Procedure. Each patient was rated on the AIMS, developed by the Psychopharmacology Research Branch of NIMH (Guy, 1976). This scale has been shown to be reliable in two separate studies (Smith et al., 1979; Chien et al., 1977). AIMS is designed to record the presence and severity of abnormal movements in seven areas of the body: Muscles of facial expression; lips and perioral area; jaw; tongue; upper extremities; lower extremities; and trunk. The scale specifically excludes ratings of tremor. A five-point severity scale is used for each body area: 0 = None; 1 = minimal/may be extreme normal; 2 = mild; 3 = moderate; and 4 = severe. Also included are items for rating the overall severity of abnormal movements (range 0–4), incapacitation due to the movements (range 0–4), and the patient's reported awareness and distress related to the abnormal movements (range 0–4).

In addition, at the time of the AIMS rating a subset (12 items) of the Coopersmith Self-Esteem Inventory (Coopersmith, 1967) was administered. The Coopersmith Self-Esteem Inventory is a 58 item self-report scale presented in dichotomous (agree/disagree) format. Finally two clinical staff members familiar with the patient completed the Nurses Observation Scale for Inpatient Evaluation (NOSIE) (Honigfeld et al., 1966) on each patient. The NOSIE is a 30 item behavior rating scale for use by nursing personnel that provides measures of six factors (Social Competence, Social Interest, Personal Neatness, Irritability, Manifest Psychosis, and Retardation). The results of the Coopersmith and the NOSIE will be reported elsewhere.

Prior to data collection three raters were trained in the use of the AIMS by rating cases on an AIMS videotape provided by the Psychopharmacology Research Branch of NIMH and comparing their ratings with those presented on the tape. In addition, the raters examined a number of inpatients previously identified as having varying degrees of tardive dyskinesia and discussed their ratings with the other project staff experienced in the use of the AIMS. To eliminate a possible source of bias raters were kept blind to the age and sex trends previously reported.

Raters worked in three separate teams of two. One rater conducted the AIMS examination and both raters made independent ratings on the AIMS at the conclusion. Modifications in the AIMS examination and rating procedure were those previously described (Smith et al., 1978, 1979). Raters alternated in conducting the examination. During the ratings the patients remained in the examination room (a distraction-free area) so that the raters could reevaluate symptoms about which they may have had some questions during the examination.

In addition to the ratings on the individual AIMS items a total score was computed by summing the ratings on the first seven items. For data analysis purposes the averages of the ratings of the two raters were computed.

Concurrent with the patient examination a review of case records was conducted by a member of the research team not involved in the rating process. The presence of other neurological conditions, present psychotropic medications prescribed, time since first inpatient hospitalization, date of birth, and psychiatric diagnosis were recorded. This information was not available to the raters until all examinations ($N = 213$) had been completed.

Results

Interrater Reliabilities. Interrater reliabilities were computed separately for each of the three rater teams and averaged using Fisher's Z function. These data are presented in Table 1. As indicated, the average interrater reliability for the total score (the sum of the first seven AIMS items) was 0.87.

Age and Sex Trends. Mean AIMS total scores for each age and sex group are presented in Table 2. With the exception that there were too few 80 year olds and above (4 males, 5 females) to form a separate age group, these were the same age/sex groupings employed in the previous inpatient study (Smith et al., 1978). The inpatient data are presented for comparison purposes. To examine trends of age and sex, two-way unweighted means analyses of variance (sex by age group) were performed on the outpatient total scores as well as on the scores of the individual AIMS items. These were the same analyses which were previously applied to the inpatient data (Smith et al., 1978).

Age was a significant factor for face ($P < 0.01$), lips ($P < 0.01$), jaw ($P < 0.01$), tongue ($P < 0.01$), lower extremities ($P < 0.05$), and total score ($P < 0.01$). In contrast to the inpatient results neither sex nor the interaction of sex with age were significant factors for any of the body areas or for total score. Orthogonal trend analyses indicated that males had significant

Sex not factor

Table 1. Interrater reliabilities of AIMS items

AIMS Item	Team 1 Raters A, B ($N = 80$)	Team 2 Raters A, C ($N = 64$)	Team 3 Raters B, C ($N = 69$)	Combined[a]
1. Muscles of facial expression	0.35	0.47	0.59	0.48
2. Lips and perioral area	0.62	0.79	0.70	0.71
3. Jaw	0.69	0.78	0.68	0.72
4. Tongue	0.75	0.87	0.64	0.77
5. Upper extremities	0.75	0.63	0.68	0.69
6. Lower extremities	0.84	0.74	0.74	0.78
7. Trunk	0.55	0.59	0.78	0.65
Total (Sum of 1–7)	0.87	0.89	0.85	0.87
8. Overall severity	0.69	0.84	0.70	0.75
9. Incapacitation	0.66	0.70	0.75	0.71
10. Awareness	0.98	1.00	0.99	0.99

[a] Combined interrater reliabilities are the mean Pearson correlations averaged over the three rater team combinations using Fisher's Z transformation

Table 2. Mean AIMS total scores by age and sex group

Outpatients			Inpatients		
Mean AIMS total score (N)			Mean AIMS total score (N)		
Age group (years)	Males	Females	Age group (years)	Males	Females
< 40	4.43 (27)	3.56 (17)	< 40	2.17 (24)	3.09 (17)
40–49	5.21 (12)	5.35 (17)	40–49	4.96 (27)	2.50 (10)
50–59	6.54 (14)	6.46 (27)	50–59	6.59 (17)	4.55 (28)
60–69	8.14 (22)	9.62 (38)	60–69	6.59 (37)	6.63 (38)
≥ 70	7.76 (21)	9.53 (18)	70–79	4.18 (30)	7.47 (35)
			≥ 80	4.30 (15)	10.17 (15)

Table 3. Prevalence (%) as a function of criterion level of symptomatology

Criterion level[a]	Inpatients ($N = 293$)			Outpatients ($N = 213$)		
	Male	Female	Mean[b]	Male	Female	Mean[b]
2.0	59.3	65.0	62.2	71.9	72.7	72.3
2.5	39.3	52.4	45.9	36.5	45.3	40.9
3.0	24.7	35.7	30.2	20.8	26.5	23.7
3.5	8.7	18.9	13.8	5.2	12.0	8.6
4.0	3.3	10.5	6.9	3.1	1.7	2.4

[a] The level of symptomatology required in at least one of the seven body areas to include a patient in the prevalence computations. Since two raters were employed, it is possible to obtain average ratings of 2.5 and 3.5 on an AIMS item

[b] Since the sample sizes are unequal the mean value presented is the average of the 2 prevalence figures

linear trends with increasing age ($P < 0.01$) on three of the seven body areas (lips, jaw, and tongue) and a significant cubic trend ($P < 0.05$) on lower extremities. Females displayed significant linear trends with increasing age ($P < 0.01$) on face, lips, jaw, tongue, and lower extremities and significant linear and cubic trends on trunk ($P < 0.05$). Both male and female groups showed significant linear increases on AIMS total score with increasing age ($P < 0.01$ in each case). The computation of t-tests between the male and female means at each age level indicated that there were no significant differences.

To determine whether there were any age and sex differences in the time since the first psychiatric hospitalization or current level of neuroleptic medication, similar two-way unweighted means analyses of variance (sex by age group) were conducted on these data. With regard to the time since first hospitalization there was a significant effect for age and for the interaction of age and sex. The computation of t-tests between males and females for each age group indicated that, for the 40–49 year age group, males had a significantly longer time since first hospitalization ($\bar{X} = 24.17$ years) than females ($\bar{X} = 11.41$ years). Chlorpromazine (CPZ) equivalents using the conversion values presented by Wyatt (1976) were available for 195 of 213 patients. As expected, the analysis of variance for these data indicated that there was a statistically significant decline in mean CPZ as a function of increasing age. There were no significant differences between males and females for any of the age groups.

Prevalence. The diagnosis of tardive dyskinesia in a given case should be based on a number of considerations including the presence of a criterion level of symptomatology (i.e., abnormal movements), prior drug history, neurological examination, time of onset of symptoms, presence of other neurological signs, and genetic history of neurological disorders to name a few.

They exclude people with 2.0 on only one symptom

However in this study, as in many other large scale prevalence studies of this disorder, it was not possible to conduct the intensive case review required to make a definitive diagnosis. Hence the selection of a criterion level of symptomatology, albeit somewhat arbitrary, is the most critical factor in determining the prevalence.

Since relatively high total scores can result from several low ratings and since relatively low total scores can result despite the rating of severe symptomatology on a single body area, it was felt to be preferable to compute prevalence figures based on the presence of a criterion level of symptomatology in at least one of the seven body areas. Table 3 presents the prevalence figures as a function of the criterion level of symptomatology selected. Data from the prior study of inpatients using the same methodology are presented for comparison purposes (Smith et al., 1979). As expected, as the criterion becomes more severe the prevalence falls sharply.

Since the prevalence figure using a 2.0 criterion appears high in contrast to previous research and since a single mean rating of 2.0 could arise from a number of habits, tics, and the like, it was felt to be useful to determine how many of this group had a mean rating of 2.0 on only one symptom. Almost one-third (28.6%) of the patients identified using this criterion had a single rating of 2.0 and none higher, suggesting that perhaps this criterion is too inclusive. In contrast, of the patients with symptomatology of 2.5 or higher on at least one symptom, only 10.2% had a single rating of 2.5 and no other symptoms rated at least mild (i.e., 2.0). On this basis it would appear that a mean rating of 2.5 would be a more appropriate criterion for establishing prevalence estimates allowing for the fact that, had the intensive case reviews been done as noted above, a certain, relatively small percentage of these would be found to be suffering from movement disorders from causes other than tardive dyskinesia, e.g., Huntington's chorea, Wilson's disease. To give some idea of the meaning of a symptom at the level of 2.5, it would be fair to say that such movements could be easily overlooked by clinical staff in their normal interactions with patients but would most surely be noted by them if they were asked to examine the patient for abnormal movements.

Since prevalence values are unstable for small samples (i.e., less than 20–30), age groups were combined to yield adequate sample sizes for the prevalence calculations. The resulting age groups were 20–49, 50–69, and 70+ years. Table 4 presents percent prevalence figures and mean AIMS total scores for these age groups using 2.5 as a criterion. The inpatient data are again presented for comparison purposes.

In both the inpatient and outpatient samples, males show a decline in prevalence for the oldest age group while females show an increase. While the outpatient prevalence values are relatively similar and even occasionally considerably below those for the comparable inpatient group, AIMS total scores for the outpatients are in most instances considerably above those of the inpatient group. Notable examples of this are found for the data of the 70+ males and of the 50–69 year old females. To examine these differences more precisely *t*-tests were conducted on AIMS total scores and chi-square analyses were performed on the prevalence values between inpatient and outpatient sample data for each of the six age/sex groups separately. The *t*-tests indicated that outpatients had significantly higher AIMS total scores for the 70+ males ($P < 0.001$), the 20–49 year old females ($P < 0.05$), and the 50–69 year old females ($P < 0.01$). In contrast, chi-square analyses of the prevalence data for these six age/sex groups indicated no significant differences in prevalence between any of the inpatient and outpatient samples.

Table 4. Mean AIMS total score and prevalence (%) as a function of age and sex

Age group (years)	Males			Females		
	N	Mean AIMS score[a] (SD)	% Prevalence[b]	*N*	Mean AIMS score[a] (SD)	% Prevalence[b]
Inpatients (N = 293)						
20–49	51	3.65 (3.19)	31.4	27	2.87 (3.10)	14.8
50–69	54	6.59 (5.31)	48.1	66	5.75 (4.06)	59.1
70+	45	4.22 (3.30)	37.8	50	8.28 (6.09)	64.0
Outpatients (N = 213)						
20–49	39	4.67 (2.43)	20.5	34	4.46 (2.84)	23.5
50–69	36	7.51 (4.50)	50.0	65	8.31 (4.77)	49.2
70+	21	7.76 (3.46)	42.9	18	9.53 (3.79)	72.2

[a] Where AIMS score is the sum of the ratings on the seven body area items
[b] Defined as a mean rating of at least 2.5 on at least one of the seven body area items

Using 2.5 rating

Discussion

The results of this investigation indicate that the prevalence of tardive dyskinesia in outpatients is similar to that found using the same methodology in inpatients (Smith et al., 1978). This was not unexpected since the sample of outpatients was composed mainly of previous long-term inpatients. However, these results are at variance with the prevalence figures reported by Asnis and associates who also used the AIMS (Asnis et al., 1977). For their younger group of outpatients (i.e., 50 years old or younger) they found a prevalence of 43.4%. In contrast, for a similar age group (20–49 years) the combined male/female prevalence in the present study is 22.0% (Table 4: Males, 20.5%; females, 23.5%). Furthermore, it is not unlikely that the patients rated by Asnis and associates received *less* neuroleptics since nearly 70% of their total sample received neuroleptic medication for less than 5 years while the time since first hospitalization for the 20–49 year old age group in the present study was 11.51 years (SD = 8.93). Aside from the possibility that these differences resulted from sampling artifacts, they suggest that Asnis et al. used a milder criterion for inclusion in the dyskinetic group than that used in the present study. This highlights the need to be explicit in defining the prevalence criteria.

The data presented also indicates that increasing age is more highly associated with the presence of tardive dyskinesia than sex. However, it must be kept in mind that age is usually correlated with duration of neuroleptic treatment.

With regard to trends of age and sex, the results, while suggestive, did not confirm the previously reported age trends in dyskinesia for the sexes (females, linear; males, curvilinear). In contrast to these previous inpatient findings, in the present study both sexes displayed linear increases with increasing age although this effect was somewhat attenuated in the male sample. Differences between the two studies may result from the reduced number of outpatients in the older age groups. However, these differences could be the result of an interaction between dyskinesia and discharge from the institution. While the physical appearance of dyskinesia itself may impede discharge other associated factors may be involved as well. Since tardive dyskinesia is thought to result from a hypersensitivity of the dopaminergic nigro-striatal tract following a period of blockade, it is conceivable that other dopamine tracts (limbic tracts for example) may also suffer from this supersensitivity resulting in increased manifestations of psychopathology in patients suffering from tardive dyskinesia. Preliminary analyses of the NOSIE data obtained in this project indicate that female patients with tardive dyskinesia are significantly lower on NOSIE factors social interest and personal neatness than female patients of comparable age without dyskinesia.

The examination of differences between the inpatient and outpatient samples in terms of AIMS total scores and prevalence estimates suggests the presence of many more marginal and mild dyskinetic movements in the outpatient sample. Such marginal and mild movements (i.e., ratings of 1.0, 1.5, and 2.0) would not meet our prevalence criterion of 2.5 but could aggregate to inflate AIMS total scores. Since different raters were used in each of these projects it is possible that these differences could be attributable to differences in the raters' frame of reference. However, this appears unlikely since the raters who rated the inpatient sample trained the outpatient raters and since the prevalence values suggest no uniform bias toward rating higher levels of severity. A more likely interpretation of this phenomenon may lie in differences in current levels of neuroleptic medication between the two samples. The outpatients were currently receiving lower levels of neuroleptic medication (mean inpatient CPZ equivalent = 422.45, mean outpatient CPZ equivalent = 302.16, $P < 0.01$), and in several of the clinics an attempt was being made to withdraw patients from medication entirely over a period of time. Hence the increased levels of mild symptomatology in the outpatients may represent withdrawal dyskinesias or tardive dyskinesias in the process of remission. Gardos et al. (1978) have recently focused attention on differentiation of the mild, completely reversible withdrawal dyskinesias from the obvious, persistent, and sometimes irreversible tardive dyskinesias.

Finally, the results of this study again support the use of the AIMS as a reliable instrument for the measurement of tardive dyskinesia. While the interrater reliability of individual items may be lower than desired, the average reliability of AIMS total scores (0.87) was satisfactory and similar to that found in two previous studies (Smith et al., 1979; Chien et al., 1977). Use of this scale in other prevalence studies would be most valuable.

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22% prevalence in younger, versus 44% (Asnis)

? uses tougher criteria = 2.5 rating

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