Eur Arch Psychiatry Clin Neurosci (1995) 245 : 145–151

ORIGINAL PAPER

Michele Raja

Tardive dystonia

Prevalence, risk factors, and comparison with tardive dyskinesia in a population of 200 acute psychiatric inpatients

Received: 29 August 1994 / Accepted: 3 February 1995

Abstract In a population of 200 consecutive inpatients with a history of at least 3 months' total cumulative neuroleptic exposure, the prevalence of tardive dystonia (TDt) was 4%, higher than previously reported. The prevalence of tardive dyskinesia (TDk) was 22%. Patients with TDt did not differ in demographic or clinical variables from nondyskinetic patients. In comparison with patients with TDk, patients with TDt were significantly younger, had a more severe movement disorder, and had received neuroleptics for the first time fewer years before. Patients with TDk were significantly older than patients without tardive disorders, both when they were examined and when they had started their first neuroleptic treatment. Furthermore, they had started their first neuroleptic treatment more years before. These results support the distinction between TDt and TDk, and suggest that the previously reported prevalence of TDt might have been underestimated.

Key words Prevalence · Risk factors · Tardive dyskinesia · Tardive dystonia

Introduction

Tardive dyskinesia (TDk) still remains a serious limitation of neuroleptic treatment. The prevalence of TDk reported in the literature varies widely depending on the different populations studied. In a recent review [71] the average TDk prevalence was estimated at 15–20%.

Older age is the only risk factor consistently confirmed by most studies. Possible predisposing factors are affective diagnosis [30, 46, 54], prior extrapyramidal syndromes [14, 32], brain damage [66], diabetes mellitus [20], use of high potency neuroleptics [31], length of treatment or lifetime dosage [31, 46], and drug holidays [25]. The importance of these variables is, however, still uncertain.

Gender and geographical differences have also been considered as possible risk factors. Yassa and Jeste [71] found the mean prevalence of TDk to be 21.5% (men 17.9%; women 24.2%) in European studies, 27.6% (men 24.9%; women 30.6%) in North American studies, 16.6% (men 17.3%; women 15.8%) in Asian studies, and 25.5% (men 25.1%; women 25.9%) in African and Middle Eastern studies.

In Italy, Muscettola et al. [47] found a persistent TDk prevalence of 19.1% in 1745 psychiatric patients (20.3% among the 1269 chronically hospitalized inpatients and 15.7% among the 476 outpatients of their sample). Altamura et al. [3] found a TDk prevalence of 32% in 148 chronic patients with a mean age of 55 years (SD = 11 years). Cavallaro et al. [11] reported a prevalence of 39.2% in 125 institutionalized schizophrenic patients receiving continuous neuroleptic treatment, with a mean age of 57.8 years. Unfortunately, most of these studies on neuroleptic-induced tardive disorders did not discriminate between TDk and Tardive dystonia (TDt).

TDt is a disorder of dystonic movements associated with long-term use of dopamine-receptor blocking agents such as antipsychotic drugs. Dystonia refers to twisting, frequently forceful contorting movements, long-sustained at the peak of the movement and often progressing to abnormal attitude or posture. Dystonic movements may be slow ("athetotic dystonia") or shock-like ("myoclonic dystonia") [16]. Although the onset of TDt generally occurs after long-term exposure to antidopaminergic drugs, an atypical onset of TDt after only a few weeks or even days of neuroleptic treatment has been reported [9].

The anatomical basis and pathopyhsiology of TDt and TDk are presently unknown. Neuroimaging studies of patients with secondary dystonia suggest a role for the basal ganglia (mainly the putamen) in the etiology of this disorder [37].

Michele Raja
Servizio psichiatrico di diagnosi e cura, Ospedale "Santo Spirito," Dipartimento di salute mentale USL RM E, Rome, Italy

M. Raja (✉)
Via Prisciano 26, CAP I-00136, Rome, Italy

As idiopathic dystonia, TDt can only occur when the affected body part is carrying out an active movement *(action dystonia)*; otherwise, TDt can only appear during movements of different body areas or can be present permanently, even at rest *(persistent dystonia)*. Regarding localization, *focal TDt* refers to abnormal movements of a simple body part, *segmental TDt* to abnormal movements of two or more contiguous body areas, *multifocal TDt* to abnormal movements of two or more noncontiguous body areas, and *generalized TDt* to dystonia of multiple, disparate parts of the body [16].

TDt has been considered a variant of TDk, however, its pathophysiology, course, outcome, and response to treatment are likely to be different [9, 12, 23, 35, 44, 58, 65]. Unlike TDk, TDt often induces discomfort or pain. Usually, functional impairment is more severe with TDt than with TDk [50]. Furthermore, the remission of TDt is rare [10]. According to some studies, patients with TDt are younger than patients suffering from other neuroleptic-induced tardive disorders, but not dystonia [24, 68]. Unlike *withdrawal TDk* [57], *withdrawal TDt* is rare. While TDk usually worsens with anticholinergic treatment, TDt may sometimes improve [16, 21, 45]. Anectodic reports suggest that a few cases of TDt may improve with tetrabenazine [33], reserpine [16], bromocriptine [42], or electroconvulsive therapy [2, 34]. Growing evidence suggests that clozapine improves TDt more than TDk [39, 43].

Several recent studies reported a prevalence of TDt of 1–2% [19, 55, 67, 69, 71]. Owens [50] hypothesizes that the disorder is, however, underestimated. According to this author, the use of rating scales better designed to rate static postural distortions, increasing awareness, and skill in recognition will lead to greater prevalence rates being reported. Up to now, most of the studies on TDt were issued from neurological departments or from movement-disorder clinics. As only severer or unusual cases tend to be referred to these centres, a distortion of the results, due to factor-neglect, seems probable in these studies. A higher prevalence of TDt, or in any case a precise estimation of this syndrome, could result from examination of an unselected neuroleptic-treated population.

The aims of the present study were: (1) to assess the prevalence of TDt and TDk in acute psychiatric patients, i.e., in patients who will need long-term neuroleptic treatment in the coming years, (2) to check patient-related variables as possible risk factors for TDt or TDk, and (3) to find out the characteristics of the patients with TDt and to compare them with the patients with TDk.

Subjects and methods

Subjects for this study were 200 consecutive inpatients with a history of at least 3 months' total cumulative neuroleptic exposure, admitted to a psychiatric emergency ward. All patients underwent a thorough clinical evaluation that included the use of the following rating scales: Brief Psychiatric Rating Scale (BPRS) [49], including 18 items rated 0 to 4 [7], Global Assessment of Functioning Scale (GAF), "current" and "past year" [4], Abnormal Involuntary Movement Scale (AIMS) [48]. Psychiatric diagnoses were made according to DSM-III-R criteria. Diagnostic assessments were based on clinical interviews, review of case notes, and family-history data. Whenever possible, patients' relatives were directly interviewed. Most of the patients included in this study had been already admitted to our ward one or more times in the past 4 years. Therefore, the longitudinal course of their psychiatric illness was known to the author and his colleagues.

For purposes of statistical analyses, the schizoaffective disorder, bipolar type, was considered part of the bipolar disorder, whereas the schizoaffective disorder, depressive type, was considered part of the depressive disorder. Neuroleptic doses were converted to chlorpromazine equivalents, and anticholinergic doses to biperidene equivalents [6].

After exclusion of alternative neurological diagnoses [26], TDk was defined using the following AIMS diagnostic criterion [28]: at least a score of 3 (i.e., presence of at least "mild" abnormal involuntary movement) in one or more body areas. The patients with dystonic movements received a TDt diagnosis according to the criteria of Burke et al. [9]. Blepharospasm (prolonged eye closure due to contractions of the orbicularis oculi muscle) was grouped with dystonia according to the suggestions of Wojcik et al. [64]. The localization of the movement disorder was defined differentiating the first four oro-facial items of the AIMS from the subsequent three truncal-limb items. According to the suggestions of Yassa et al. [70], the severity criterion of one body area was chosen as a measure of severity. The psychiatric assessment always preceded the neurological examination of the patients.

In order to permit the examination of the patients who were hostile or combative in the first days of hospitalization, rating sessions had to occur after a variable period of patients' permanence in the ward. In many cases it was not possible to acquire reliable data concerning past drug treatment, except the patients' age at their first neuroleptic administration. The patients and their relatives seldom agreed about the patient's age at onset of the disorder, especially when it had been insidious. Therefore, this variable was not considered. Statistical analysis was conducted by means of *t*-test with the Bonferroni correction on continuous variables and with χ^2 test on categorical variables ($P < 0.05$ was considered to be statistically significant).

Results

Demographic and clinical features of the patients

In this sample 79 were males and 121 were females. All patients were caucasian except 2. In comparison with men, women had a higher mean age (44.7 years, SD 13.5, vs 37.7 years, SD 11.6; $P < 0.001$), received a higher percentage of affective diagnoses (42.1 vs 22.8%; $P = 0.008$), and a lower percentage of schizophrenic diagnoses (38.0 vs 54.4%; $P = 0.033$), showed better functioning (GAF "current" 27.3, SD 9.5, vs 23.0, SD 7.7; $P = 0.017$; GAF "past year" 44.0, SD 14.3, vs 37.0, SD 12.7; $P < 0.001$), and received lower neuroleptic daily doses (427 mg, SD 357.6, vs 610.8 mg, SD 472.6; $P = 0.002$).

Prevalence, localization, and severity of TDt and TDk

TDt was present in 8 patients (4%; 5 males and 3 females) and TDk in 44 patients (22%; 16 males and 28 females). Regarding localization, in the TDt group 3 patients (37.5%) had TDt in the oro-facial area, 3 patients (37.5%) in the limb-truncal area, and 2 patients (25.0%) both in the oro-facial and the limb-truncal area. In the

TDk group, 31 patients (70.5%) had TDk in the oro-facial area (13 males and 18 females), 7 patients (15.9%) in the limb-truncal area (3 males and 4 females), and 6 patients (13.6%) in both the oro-facial and the limb-truncal area (6 females).

Regarding severity, in the TDt group the movement disorder was moderate in 3 patients (37.5%) and severe in 2 patients (25.0%). In the TDk group the movement disorder was moderate in 14 patients (31.8%) and severe in 1 patient (2.3%). Overall, among the 52 patients with a tardive disorder (21 males and 31 females), 16 patients (30.8%) had moderate TDk or TDt (4 males and 12 females), and 3 patients (5.8%; 2 males and 1 female) had severe TDk or TDt (Tables 1 and 2).

Risk factors for TDt and TDk

Patients with TDt did not differ from nondyskinetic patients in age, educational period, GAF or BPRS scores, current neuroleptic or anticholinergic dose, time since first neuroleptic treatment, and age at first neuroleptic treatment (data not shown). Patients with TDt were significantly younger than patients with TDk (mean age 37.8 years, SD 14.5, vs 50.1 years, SD 13.2; $P < 0.05$) and received a higher mean AIMS score (4.1, SD 0.6, vs 3.3, SD 0.5; $P < 0.05$). Furthermore, in comparison with patients with TDk they had started their first neuroleptic treatment fewer years before (6.6, SD 2.6, vs 15.4, SD 8.9; $P < 0.05$).

As compared with patients without tardive disorders, patients with TDk were significantly older both at the time of this study (50.1 years, SD 13.2, vs 39.7 years, SD 12.2; $P < 0.05$) and at the moment of their first neuroleptic treatment (34.3 years, SD 12.7, vs 28.7 years, SD 10.0; $P < 0.05$); they had started their first neuroleptic treatment more years before (15.4 years, SD 8.9, vs 11.0 years, SD 8.1; $P < 0.05$). Furthermore, they showed less psychotic symptoms (measured by the BPRS items: conceptual disorganization, hostility, suspiciousness, hallucinatory be-

Table 1 Tardive dyskinesia in the different diagnostic groups. A Oro-facial tardive dyskinesia; B Limb-truncal tardive dyskinesia; m moderate; s severe

Shown for each category one total number of cases with tardive dyskinesia; first number in parentheses represents males; second number represents females

Diagnosis	A or B	A	B	A and B	A (m)	A (s)	B (m)
Schizophrenia	18 (10; 8)	13 (8; 5)	4 (2; 2)	1 (0; 1)	1 (0; 1)	0	2 (1; 1)
Bipolar disorder	14 (3; 11)	11 (2; 9)	2 (1; 1)	1 (0; 1)	5 (0; 5)	0	1 (0; 1)
Depressive disorder	6 (1; 5)	2 (1; 1)	0	4 (0; 4)	2 (0; 2)	1 (0; 1)	1 (0; 1)
Atypical psychosis	2 (2; 0)	2 (2; 0)	0	1 (1;0)	1 (1; 0)	0	0
Mental retardation	2 (0; 2)	1 (0; 1)	1 (0; 1)	0	0	0	0
Personality disorder	2 (0; 2)	2 (0; 2)	0	0	1 (0; 1)	0	0
All	44 (16; 28)	31 (13; 18)	7 (3; 4)	6 (0; 6)	10 (1; 9)	1 (0; 1)	4 (1; 3)

Table 2 Tardive dystonia in the different diagnostic groups

Note: Same definitions as Table 1

Diagnosis	A or B	A	B	A and B	A (m)	A (s)	A & B m
Schizophrenia	5 (3; 2)	2 (1; 1)	2 (1; 1)	1 (1; 0)	1 (0; 1)	1 (1; 0)	1 (1; 0)
Bipolar disorder							
Depressive disorder							
Atypical psychosis	1 (1; 0)		1 (1; 0)				
Mental retardation	1 (1; 0)			1 (1; 0)		1 (1; 0)	
Personality disorder							
Organic psychosis	1 (0; 1)	1 (0; 1)			1 (0; 1)		
All	8 (5; 3)	3 (1; 2)	3 (2; 1)	2 (2; 0)	2 (0; 2)	2 (2; 0)	1 (1; 0)

havior, and unusual thought content; 4.2, SD 3.0, vs 5.7, SD 3.6), had fewer educational years (8.5; SD 4.0, vs 10.1, SD 4.0), and received a lower neuroleptic dose on the day of AIMS rating (401.1, SD 364.9, vs 504.1, SD 409.7). However, these last three differences failed to reach statistical significance.

On the contrary, no difference between patients with and without TDk resulted in the GAF score, the BPRS total score, the BPRS "negative symptoms" score (measured by the BPRS items: emotional withdrawal, psychomotor retardation, and blunted affect), and the anticholinergic dose on the day of AIMS rating. Psychiatric diagnosis was not associated with increased TDt or TDk risk.

Clinical features of dystonic patients

Eight of the 52 patients with tardive disorders (15.4%) showed dystonic features and received a diagnosis of TDt. They had the following main clinical features:

1. Multifocal persistent dystonia in a 27-year-old schizophrenic man: mild dystonic movements of fingers and toes; minimal incapacitation due to abnormal movements. The patient was aware of his abnormal movement, with no distress. Minimal akathisia and mild parkinsonian tremor were present.
2. Generalized persistent dystonia in a 61-year-old schizophrenic man: moderate dystonic movements of face, neck, trunk, hands, and fingers. The movement disorder lightly impaired patient's global functioning; however, the distorted position of his body and the forceful contorting movements of his arms gave him an awkward and graceless appearance. The patient was aware of his abnormal movements with mild distress. He was also affected by tonic-clonic generalized seizures. Minimal rigidity and mild postural tremor were present.
3. Focal action dystonia in a 22-year-old schizophrenic man: extremely severe lingual dystonia; dramatic functional impairment: language was not intelligible; eating was difficult. His face had a grotesque and repellent appearance [52].
4. Segmental dystonia in a 29-year-old schizophrenic black woman: mild dystonic postures of her fingers and left arm during walking. Functional impairment was minimal. The patient was unaware of her movement disorder. Minimal akinesia was present.
5. Focal persistent dystonia in a 58-year-old schizophrenic woman: moderate, intermittent right blepharospasmos (copresence of moderate lingual TDk). Incapacitation due to abnormal movements was mild, because multiple cognitive deficits of uncertain pathogenesis by themselves severely affected the patient's functioning. Two daughters of the patient were affected by mild mental retardation or by borderline intellectual functioning. The patient showed minimal akinesia and mild postural tremor.
6. Focal persistent dystonia in a 32-year-old drug-abusing woman with personality disorder: moderate bilateral blepharospasmos. This patient reported that blepharospasmos had been severer in the past. She claimed to have been "almost blind" for several months 2 years before. Her blepharospasmos had improved later, after clonazepam treatment and neuroleptic withdrawal. The patient was aware of her movement disorder with severe distress. Minimal akinesia was present.
7. Focal dystonia in a 40-year-old man with an atypical psychosis and mild mental retardation: mild dystonic postures of the fifth finger of his left hand (copresence of moderate facial and perioral TDk). No awareness was present. Incapacitation due to TDt was minimal, whereas incapacitation due to TDk was moderate. Mild akinesia and mild postural tremor were present.
8. Multifocal persistent dystonia in a 34-year-old man with moderate mental retardation and severe behavioral disorder: moderate atetosic movements of fingers and severe buccal dystonia. Incapacitation was severe. He was aware of his movement disorder, with severe distress. Mild akinesia and minimal rigidity were present.

Table 3 shows the differences between patients with TDt and patients with TDk.

Table 3 Comparison between tardive dyskinesia (TDk) and tardive dystonia (TDt) BPRS Brief Psychiatric Rating Scale; AIMS Abnormal Involuntary Movement Scale; GAF Global Assessment of Functioning Scale

	Patients with TDk ($n = 44$)	Patients with TDt ($n = 8$)	t ($df = 50$)	P
Age (years; ± SD)	50.1 (± 13.2)	37.8 (± 14.6)	2.567	< 0.05
AIMS score (± SD)	3.3 (± 0.5)	4.1 (± 0.6)	3.014	< 0.05
Age at onset of first neuroleptic therapy (± SD)	34.3 (± 12.7)	31.1 (± 14.0)	0.765	NS
Years of education (± SD)	8.5 (± 4.0)	10.7 (± 4.0)		NS
GAF (± SD; actual)	27.6 (± 10.3)	24.7 (± 8.8)		NS
BPRS total score (± SD)	13.5 (± 4.8)	13.8 (± 5.2)		NS
Psychotic factor BPRS score (± SD)	4.2 (± 3.0)	3.5 (± 1.8)		NS
Negative symptoms BPRS score (± SD)	3.1 (± 2.2)	3.6 (2.8)		NS
Chlorpromazine equivalent dose (± SD)	401.1 (± 364.9)	326.3 (± 388.1)		NS
Biperidene equivalent dose (±SD)	1.1 (± 2.0)	0.7 (± 1.5)		NS
Years since first neuroleptic treatment	15.4 (± 8.9)	6.6 (± 2.6)	2.799	< 0.05

Note: Mean values (± SD) are presented; drug doses in mg

Discussion

Demographic and clinical features of patients

In this population women outnumbered men because the male subjects of a sector of our catchment area receive psychiatric assistance in another hospital. The longer average life span in women can partially account for the higher mean age of female patients in this sample. Only 7 patients were over 70 years and they were all females. Another reason could be the younger age of schizophrenic males at their first admission.

The higher percentage of schizophrenic diagnoses in men is consistent with the reported bias in selection or involvement of schizophrenic patients in research [62]. According to some authors, schizophrenic males are overrepresented in inpatient units, because they have their first admission at younger ages and have more and longer hospitalizations than females [5, 18, 27, 40]. Furthermore, current stricter diagnostic criteria for schizophrenia favor selection of schizophrenic males [41, 63], possibly reflecting an actual higher prevalence of schizophrenia in the male population, according to Kraepelin's suggestion that schizophrenia is predominantly a disorder of young men [38]. The diagnostic differences between women and men can account for the better functioning and the current lower neuroleptic dosage in women.

Prevalence and risk factors for TDt and TDk

In this population with a mean age of 41.9 years (SD 13.2), the prevalence of TDk was consistent with the data reported in the literature, whereas the prevalence of TDt was 4%, higher than previously reported. According to several authors [13, 50] TDt could have been underrecognized. During a single examination, the diagnosis of an early or mild form of extrapyramidal disorders may be difficult or questionable. Furthermore, it may be more difficult to diagnose mild TDt than mild TDk, because the irregular, rapid, jerky movements of TDk are easier to distinguish from the patient's normal posture or movement than the abnormally sustained posturing of TDt. In 2 of our dystonic patients (no. 4 and no. 7), mild dystonia was present during active movements of other body areas. These particular cases could have been overlooked in an occasional neurological examination, but I had several opportunities to observe these inpatients in our psychiatric intensive care unit.

In the TDk group age was the strongest risk factor. Although female patients were significantly older, they did not differ from men in the relative frequency of TDk and TDt. The mean odds ratio of the relative risk of TDk in women to that in men reported by Yassa and Jeste [71] was 1.3. However, they emphasized that this odds ratio had decreased from 1.6 during the 1960s to 1.2 during the 1980s, although many studies found that women assessed were older than men. Yassa and Jeste [71] suggest to refer this trend to a major diagnostic shifting from schizophrenia to mood disorders in female patients, leading to a more restrictive use of neuroleptics in psychotic females. Patients with TDk started their first neuroleptic treatment at a significantly older age than the non-dyskinetic patients. Yassa et al. [68] think that the risk of TDk might increase if neuroleptic treatment is delayed after the onset of psychosis. The present study cannot test this hypothesis, because reliable information could not be obtained about the onset of the psychiatric disorder of many patients. The mean score of the BPRS "psychotic factor" in patients with TDk was nonsignificantly lower than in patients without tardive disorders, possibly reflecting less acute exacerbations in older patients or in later stages of disease.

The masking effect of the neuroleptics on milder TDk or a more cautious approach to the neuroleptic therapy in patients with TDk and in older patiens can account for the somewhat higher mean neuroleptic dosage as compared with patients without tardive disorders. Patients with TDk had fewer educational years than patients without tardive disorders, although the difference was not statistically significant. An earlier onset of their psychotic disorders is unlikely to account for this difference, because patients with TDk were older than nondyskinetic patients when they had started their first neuroleptic treatment. The education level on its own could influence dyskinetic symptoms as well as behavioral disorders in psychiatric patients. Many studies have consistently associated cognitive dysfunction to TDk [8, 15, 17, 46, 59–61]. Unfortunately, the examination of these patients did not include the assessment of their cognitive competence, and we do not know whether patients with TDk had severer cognitive dysfunction. Furthermore, the cross-sectional nature of the present study does not allow to infer any causal relationship between time-associated variables.

Comparison between TDt and TDk

The results of this study show significant differences between TDt and TDk. In accordance with previous reports [9, 53, 64, 70], dystonic patients tended to be younger, male, with a shorter history of exposure to neuroleptics, and with a severer form of movement disorder as compared with patients with TDk. On the contrary, the study of Sachdev [56] found that TDt and TDk do not differ in these putative risk factors, and suggested that a history of postural tremor prior to the onset of the mental disorder and the development of a dystonia as an acute side effect of neuroleptics might be risk factors for TDt.

In comparison with patients with TDk, our patients with TDt were significantly younger, were more severely affected, and had taken neuroleptics for the first time fewer years before. All these differences were statistically significant. However, the last one should be interpreted with caution, because information about first neuroleptic treatment was obtained retrospectively.

Whereas only 14 of 30 patients with TDk had a moderate or severe movement disorder, among the 8 dystonic

patients, 3 had a moderate and 2 a severe form of TDt. My colleagues and I were impressed by the young age and the extreme severity of cases 3, 6, and 8, which contrasted strikingly with typical TDk cases.

Although they were more severely affected, paradoxically patients with TDt were, more than patients with TDk, similar in demographic and clinical variables to controls without tardive disorders. This result suggests the possibility that individual pretreatment vulnerability plays a major role in TDt. Two patients showed both TDk and TDt. Nearly all studies on TDt report its overlapping with TDk, making the boundaries between them uncertain. Generally, the phenomenology of movement disorder does not always allow clearcut distinction between different diseases. Adams and Victor [1] emphasize that the classifical differences between chorea and athetosis, or between athetosis and dystonia, may be more apparent than real, and that in clinical practice, all types of involuntary movement may be combined in a "gestalt" of dyskinesias. Nevertheless, the clinical distinction of chorea, athetosis, ballismus, and dystonia proved to be of heuristic value.

Although presently data from empirical studies cannot settle the question of whether TDt is a variant of TDk or a separate syndrome, there is growing evidence that TDt and TDk should be clearly differentiated. On these grounds, in the section "Other Conditions That May Be a Focus of Clinical Attention," DSM-IV leaves TDt out of the TDk group.

Severe tardive disorders

In this sample most of the patients with tardive disorders showed mild abnormal movements and only 3 subjects (1.5%) showed severe symptoms and critical functional impairment. These results are consistent with previous studies that pointed out an approximately 1% prevalence of severe and irreversible dyskinetic symptoms [22, 29]. Unfortunately, it seems presently impossible to identify patients at high risk for severe tardive disorders.

Because schizophrenia or other severe mental disorders affect patients more than TDk or TDt, the risk of these tardive disorders should not preclude long-term administration of neuroleptics to treat or prevent relapses, unless more specific and safer therapies are feasible [36]. Even in the patient of this sample, most severely affected by TDt, the major clinical problem was his behavioral disorder related to schizophrenic illness.

In conclusion, this study points out a higher prevalence of TDt than previously reported, and some clinical differences between TDt and TDk. However, no demographic or clinical differences resulted between patients without tardive disorders and patients with TDt. Studies on larger samples could identify risk factors for this serious side effect, whereas genetic studies on the hereditary dystonias could help to understand the nature of this movement disorder. In many families affected by idiopathic torsion dystonia, a mutation of the DYT1 gene on chromosome 9q34 has already been identified [51]. The reverse genetic approach is likely to specify the anatomical or neurochemical basis of this disorder. This could clarify the pathogenesis of secondary dystonias, the most frequent of which is TDt.

Acknowledgement The author thanks Dr. Erika Gsell for her help in the revision of the English text.

References

1. Adams RD, Victor M (1993) Principles of neurology, 5th edn. McGraw-Hill, New York, pp 71–72
2. Adityanjee, Jayaswal SK, Chan TM, Subramaniam M (1990) ECT for tardive dystonia. Br J Psychiatry 156:433–435
3. Altamura AC, Cavallaro R, Regazzetti MG (1990) Prevalence and risk factors for tardive dyskinesia: a study in an Italian population of chronic schizophrenics. Eur Arch Psychiatry Clin Neurosci 240:9–12
4. American Psychiatric Association (1987) Diagnostic and statistical manual of mental disorders (DSM-III-R) 3rd edn, revised. American Psychiatric Press, Washington, DC
5. Angermeyer MC, Kuhn L, Goldstein JM (1990) Gender and the course of schizophrenia: differences in treated outcome. Schizophr Bull 16:293–307
6. Baldessarini RJ (1985) Chemotherapy in psychiatry: principles and practice. Harvard University Press, Cambridge, Mass
7. Bech P, Kastrup M, Rafaelsen OJ (1986) Minicompendium of rating scales. Acta Psychiatr Scand 73 (Suppl 326)
8. Brown KW, White T (1991) The psychological consequences of tardive dyskinesia. Br J Psychiatry 159:399–403
9. Burke RE, Fahn S, Jankovic J et al. (1987) Tardive dystonia: late onset and persistent dystonia caused by antipsychotic drugs. Neurology 32:1335–1346
10. Burke RE, Kang UJ (1988) Tardive dystonia: clinical aspects and treatment. In: Fahn S et al (eds) Advances in neurology. Raven Press, New York, 49:199–210
11. Cavallaro R, Regazzetti MG, Mundo E, Brancato V, Smeraldi E (1993) Tardive dyskinesia outcomes: clinical and pharmacologic correlates of remission and persistence. Neuropsychopharmacology 8:233–239
12. Casey DE (1987) Tardive dyskinesia. In: Meltzer HY (ed) Psychopharmacology: the third generation of progress. Raven Press, New York
13. Chiu H, Shum P, Lau J, Lam L, Lee S (1992) Prevalence of tardive dyskinesia, tardive dystonia, and respiratory dyskinesia among Chinese psychiatric patients in Hong Kong. Am J Psychiatry 149:1081–1085
14. Chouinard G, Annable L, Mercier P, Ross-Chouinard A (1986) A five-year follow-up study of tardive dyskinesia. Psychopharmacol Bull 22:259–263
15. Davis EJB, Borde M, Sharma LN (1992) Tardive dyskinesia and type II schizophrenia. Br J Psychiatry 160:253–256
16. Fahn S (1987) Drug treatment of hyperkinetic movement disorders. Semin Neurol 7:192–208
17. Famuyiwa OO, Eccleston D, Donaldson AA, Garside RF (1979) Tardive dyskinesia and dementia. Br J Psychiatry 135:500–504
18. Flor-Henry P (1990) Influence of gender in schizophrenia as related to other psychopathological syndromes. Schizophr Bull 16:211–227
19. Friedman JH, Kuraski LT, Wagner RI (1987) Tardive dystonia in a psychiatric hospital. J Neurol Neurosurg Psychiatry 50:801–803
20. Ganzini L, Heintz RT, Hoffman WF, Casey DE (1991) The prevalence of tardive dyskinesia in neuroleptic-treated diabetics. Arch Gen Psychiatry 48:259–263
21. Gelenberg AJ (1987) Treating extrapyramidal reactions: some current issues. J Clin Psychiatry (Suppl 9):24–27

22. Gerlach J, Casey DE (1988) Tardive dyskinesia. Acta Psychiatr Scand 77:369–378
23. Gershanik OS (1993) Drug-induced movement disorders. Curr Opin Neurol Neurosurg 6:369–376
24. Gimenez-Roldan S, Mateo D, Bartolome P (1985) Tardive dystonia and severe tardive dyskinesia. Acta Psychiatr Scand 71: 488–494
25. Goldman MB, Luchins DJ (1984) Intermittent neuroleptic therapy and tardive dyskinesia: a literature review. Hosp Comm Psychiatry 35:1215–1219
26. Granacher RP (1981) Differential diagnosis of tardive dyskinesia: an overview. Am J Psychiatry 138:1288–1297
27. Harris MJ, Jeste DV (1988) Late-onset schizophrenia: an overview. Schizophr Bull 14:39–55
28. Jeste DV, Wyatt RJ (1982) Understanding and treating dyskinesia. The Guildford Press, New York
29. Kane JM (1987) Treatment of schizophrenia. Schizophr Bull 13:133–156
30. Kane JM, Struve FA, Weinhold P (1980) Strategy for the study of patients at high risk for tardive dyskinesia. Am J Psychiatry 137:1265–1267
31. Kane JM, Woerner M, Lieberman J (1985) Tardive dyskinesia: prevalence, incidence and risk factors. In: Casey DE, Chase T, Christensen AV, Gerlach J (eds) Dyskinesia research and treatment. Psychopharmacology (Suppl 2). Springer, Berlin Heidelberg New York, pp 72–78
32. Kane JM, Woerner M, Borenstein M, Wegner J, Lieberman J (1986) Integrating incidence and prevalence of tardive dyskinesia. Psychopharmacol Bull 22:254–258
33. Kang UJ, Burke RE, Fahn S (1986) Natural history and treatment of tardive dystonia. Mov Disord 1:193–208
34. Kaplan Z, Benjamin J, Zohar J (1991) Remission of tardive dystonia with ECT. Convulsive Ther 7:280–283
35. Keegan DL, Rajput AH (1973) Drug-induced dystonia tarda: treatment with L-dopa. Dis Nerv Syst 38:167–169
36. Kissling W (1992) Ideal and reality of neuroleptic relapse prevention. Br J Psychiatry 161 (Suppl 18):133–139
37. Korczyn AD, Inzelberg R (1993) Dystonia. Curr Opin Neurol Neurosurg 6:350–357
38. Kraepelin EL (1919) Textbook of Psychiatry, vol 3: dementia praecox. McMillan, London
39. Lamberti JS, Bellnier T (1993) Clozapine and tardive dystonia. J Nerv Ment Dis 181:137–138
40. Lewine RRJ (1981) Sex differences in schizophrenia: timing or subtypes. Psychol Bull 90:432–444
41. Lewine RRJ, Burbach D, Meltzer HY (1984) The effect of diagnostic criteria on the proportion of male to female schizophrenics. Am J Psychiatry 141:84–87
42. Lieberman JA, Alvir J, Mukherjee S, Kane JM (1989) Treatment of tardive dyskinesia with bromocriptine. Arch Gen Psychiatry 46:908–913
43. Lieberman JA, Saltz BL, Johns CA, Pollack S, Borenstein M, Kane J (1991) The effects of clozapine on tardive dyskinesia. Br J Psychiatry 158:503–510
44. Luchins D, Goldman M (1985) High dose bromocriptine in a case of tardive dystonia. Biol Psychiatry 20:179–181
45. Marsden CD, Quinn NP (1990) The dystonias. Br Med J 300: 139–144
46. McClelland HA, Metcalfe AV, Kerr TA et al (1991) Facial dyskinesia: a 16-year follow-up study. Br J Psychiatry 158: 691–696
47. Muscettola G, Pampallona S, Barbato G et al (1989) Tardive dyskinesia in Italy: preliminary findings. Arch Gen Psychiatry 46:754–755
48. NIHM, Psychopharmacology Research Branch (1986) Psychopharmacol Bull 24:781–782
49. Overall JE, Gorhan DR (1962) The Brief Psychiatric Rating Scale. Psychol Rep 10:799–812
50. Owens DGC (1990) Dystonia – a potential psychiatric pitfall. Br J Psychiatry 156:620–634
51. Ozelius LJ, Kramer PL, De Leon D, Rish N, Bressman SB, Schuback DE, Brin ME, Kwiatkowski DJ, Burke RE, Gusella JF, Fahn S, Breakfield XO (1992) Strong allelic association between the Torsion dystonia gene (DYT1) and loci on chromosome 9q34 in Ashkenazi Jews. Am J Human Genet 50:619–628
52. Raja M, Altavista MC, Maisto G (1994) Severe tardive lingual dystonia. In: Focus on dystonia. A Satellite Meeting of the 11th Parkinson's Disease Symposium, Rome, March 25, 1994. Abstract book P04, p 34
53. Roller WC (1988) Tardive dystonia: diagnosis and treatment. In: Wolf ME, Mosnaim AD (eds) Tardive dyskinesia: biological mechanisms and clinical aspects. American Psychiatric Press, Washington, DC
54. Rush M, Diamond F, Alpert M (1982) Depression as a risk factor in tardive dyskinesia. Biol Psychiatry 17:387–392
55. Sachdev P (1991) The prevalence of tardive dystonia in patients with chronic schizophrenia (letter). Aust N Z J Psychiatry 25:446–448
56. Sachdev P (1993) Risk factors for tardive dystonia: a case-control comparison with tardive dyskinesia. Acta Psychiatr Scand 88:98–103
57. Schooler NR, Kane JM (1982) Research diagnoses for tardive dyskinesia. Arch Gen Psychiatry 39:486–487
58. Thaker GK, Nguyen JA, Strauss ME, Jacobson R, Kaup BA, Tamminga CA (1990) Clonazepam treatment of tardive dyskinesia: a practical GABA mimetic strategy. Am J Psychiatry 147:445–451
59. Waddington JL, Youssef HA (1986) An unusual cluster of tardive dyskinesia in schizophrenia: association with cognitive dysfunction and negative symptoms. Am J Psychiatry 143:1162–1165
60. Waddington JL, Youssef HA, Dolphim C, Kinsella A (1987) Cognitive dysfunction, negative symptoms, and tardive dyskinesia in schizophrenia. Arch Gen Psychiatry 44:907–912
61. Waddington JL, Youssef HA (1988) The expression of schizophrenia, affective disorder and vulnerability to tardive dyskinesia in an extensive pedigree. Br J Psychiatry 153:376–381
62. Wahl OF, Hunter J (1992) Are gender effects being neglected in schizophrenia research? Schizophr Bull 18:313–317
63. Westermeyer JF, Harrow M (1984) Prognosis and outcome using broad (DSM-II) and narrow (DSM-III) concepts of schizophrenia. Schizophr Bull 10:624:637
64. Wojcik JD, Falk WE, Fink JS et al (1991) A review of 32 cases of tardive dystonia. Am J Psychiatry 148:1055–1059
65. Wolf ME, Mosnaim AD (1984) Identifying subtypes of tardive dyskinesia. Hosp Community Psychiatry 35:828–830
66. Yassa R, Nair V, Schwartz G (1984) Tardive dyskinesia: a two-year follow-up study. Psychosomatics 25:852–855
67. Yassa R, Nair V, Dimitry R (1986) Prevalence of tardive dystonia. Acta Psychiatry Scand 73:629–633
68. Yassa R, Nair V, Schwartz G (1986) Early versus late onset psychosis and tardive dyskinesia. Biol Psychiatry 21:1291–1297
69. Yassa R, Nair V, Iskandar H (1989) A comparison of severe tardive dystonia and severe tardive dyskinesia. Acta Psychiatr Scand 80:155–159
70. Yassa R, Nair NPV, Iskandar H, Schwartz G (1990) Factors in the development of severe forms of tardive dyskinesia. Am J Psychiatry 147:1156–1163
71. Yassa W, Jeste DV (1992) Gender differences in tardive dyskinesia: a critical review of the literature. Schizophr Bull 18: 701–715