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Cognitive Dysfunction in Schizophrenia: Organic Vulnerability Factor or State Marker for Tardive Dyskinesia?

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The literature on the putative association between cognitive dysfunction in schizophrenia and the presence of tardive dyskinesia is critically reviewed, focusing on potential artifacts and specific relationships to a particular topography of involuntary movements. These issues are exemplified via a study of cognitive function in 64 schizophrenic patients, in which impaired cognitive flexibility was identified as the primary measure distinguishing those with tardive orofacial dyskinesia. The significance of such an association with cognitive dysfunction is considered in relation to competing hypotheses of organic vulnerability to vs. state marker for this movement disorder.

INTRODUCTION

The emergence of abnormal, involuntary movements late in the course of long-term treatment with antipsychotic drugs raises a number of clinical and ethical issues that continue to attract considerable attention. Critically, over 30 years of research has failed to establish why some patients, but not others, go on to develop tardive dyskinesia when prescribed neuroleptics on a long-term basis. There is no consistent body of evidence that patients with tardive dyskinesia have received more prolonged or more vigorous treatment with such drugs than have those who remain unaffected, and much current interest centers therefore on vulnerability factors within patients on an individual basis (Kane & Smith, 1982; Waddington, 1989).

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Perhaps the most consistent finding from research on tardive dyskinesia is a general association with increasing age (Smith & Baldessarini, 1980; Waddington, 1987), and the most widely considered (but unconfirmed) specific vulnerability factor that of preexisting organic brain dysfunction. In one of the first systematic studies on this issue, Edwards (1970) reported that signs of organicity, defined in terms of neuropsychological test performance, occurred more frequently in a group of elderly chronically ill and neuroleptic-exposed female inpatients with persistent oral dyskinesia than in a group of otherwise similar patients without such movement disorder. However, organicity is a heterogeneous notion that can be inferred on a number of differing bases, including not only cognitive impairment but also neurological signs, electroencephalographic (EEG) changes or neuroradiological abnormalities; thus, while the classical literature on organicity in patients with vs. without tardive dyskinesia is inconclusive, it involves multifarious indices of organicity in often diagnostically heterogeneous populations (Kane & Smith, 1982). The purposes of the present article are (i) to review recent studies on cognitive dysfunction in tardive dyskinesia, focusing on the disorder for which neuroleptics are most commonly prescribed, (ii) to exemplify an association between cognitive dysfunction and tardive dyskinesia, and (iii) to reevaluate the significance of such associations for the pathophysiology of this movement disorder.

THE PUTATIVE ASSOCIATION BETWEEN COGNITIVE DYSFUNCTION AND TARDIVE DYSKINESIA IN SCHIZOPHRENIA

Among purported indices of organicity, that which has been reported most consistently to distinguish populations of schizophrenic patients with tardive dyskinesia from those without such movement disorder is cognitive impairment. In Table 1 are listed recent systematic studies of neuropsychological test performance in schizophrenic patients with and without tardive dyskinesia; of the 28 studies identified, 22 have reported patients with tardive dyskinesia to be more impaired on at least one cognitive measure. Though the generally greater difficulty in publishing negative studies might tend to bias such a metaanalysis of the literature,

TABLE 1
Cognitive Function in Schizophrenic Patients with and without Tardive Dyskinesia

Study	Age[a]	Association with tardive dyskinesia
Famuyiwa et al., 1979	49 ± 5	↓ Paired associate learning
Owens & Johnstone, 1980	60 + ?	↓ Functions of the sensorium
Donnelly et al., 1981	22–72	↓ Perceptual function
Itil et al., 1981	52–88	↓ Orientation and memory
Struve & Wilner, 1983	32 + ?	↓ Abstracting ability
Bartels & Themelis, 1983	66 + 10	↓ Visual retention[b]
Wolf et al., 1983	54 ± 8	NS Memory and verbal learning
Waddington et al., 1985 Waddington & Youssef, 1986a	68 + 14	↓ Orientation and memory[b]
Wegner et al., 1985a	27 + 4	↓ Abstraction and visuomotor tracking
Richardson et al., 1985	31 + ?	NS Orientation and memory
Spohn et al., 1985	18–55	↓ Eyetracking and reaction time[b]
Waddington & Youssef, 1986b	63 ± 5	↓ Orientation and memory[b]
Waddington & Youssef, 1986c	61 ± 8	↓ Orientation and memory[b]
Thomas & McGuire, 1986	51 + 10	↓ Memory quotient
Kolakowska et al., 1986	37 ± 12	NS Neuropsychological battery
Wade et al., 1987	45 + 12	↓ Neuropsychological battery
Hoffman et al., 1987	62 ± 6	NS Neuropsychological battery
Sorokin et al., 1988	47 ± 11	↓ Visual memory[b]
DeWolfe et al., 1988	55 + 11	↓ Memory function[b]
Tegeler et al., 1988	42 + 10	↓ Visual conceptual function
Gureje, 1988	37 + 10	NS Orientation and memory
Wade et al., 1989	38 ± 10	↓ Neuropsychological battery
O'Callaghan et al., 1990	36 + 5	↓ Cognitive flexibility[b]
Manschreck et al., 1990	40 + 13	↓ Intellectual function
Karson et al., 1990	69 + 6	↓ Orientation, attention, and memory[b]
Sandyk & Kay, 1991	63 + 8	NS Orientation and memory
King et al., 1991	44 ± 12	↓ Orientation, awareness, and memory
Davis et al., in press	47 ± 12	↓ Orientation, attention, and memory[b]

Note. NS, no significant association found.
[a] Mean age ± *SD* or range.
[b] Relationship with orofacial dyskinesia specified.

the weight of positive findings nonetheless suggests a phenomenon of some consistency.

As not all studies have indicated a positive relationship, factors which might influence the reliability of any such finding are of some considerable interest. The association has been reported using a very broad range of neuropsychological test procedures, applied to a wide variety of patient populations in terms of age and chronicity, and no specific or localizing cognitive deficit is apparent; indeed, the association appears most consistent in, though by no means restricted to, older chronically ill inpatient

populations with a mean age ≥55 years (see Waddington, 1987, 1989) whose cognitive function has been evaluated using unsophisticated procedures appropriate for the generally severe level of their debilities. Two studies of specialized cognitive functions in schizophrenic patients with and without tardive dyskinesia (Collerton, Fairbairn, & Britton, 1985; Myslobodsky, Tomer, Holden, Kempler & Sigal, 1985) are not included in Table 1, as both utilized a screening procedure to exclude patients with those very forms of cognitive deficit that were associated with such movement disorder in other studies.

Regarding potential medication artifacts, the effects of neuroleptics on cognitive processes have been the subject of two recent reviews which conclude that chronic administration of such drugs does not have a major, generalized effect to impair neuropsychological performance and that higher cognitive function may be particularly spared (King, 1990; Cassens, Inglis, Appelbaum, & Gutheil, 1990); the relationship between cognitive dysfunction and tardive dyskinesia remains robust in those positive studies that have been able to control for possible confounding influences of age, duration of illness, extent of past and current exposure to neuroleptics, and potential performance deficits associated with drug/disease-related movement disorder(s). There is clearly the possibility of a confounding influence of anticholinergic medication on cognitive function, when given as an adjunct to neuroleptic therapy; however, the relationship between cognitive impairment and tardive dyskinesia again appears to remain robust in those positive studies that have been able to control for such a potential confound. In the negative study of Sandyk & Kay (1991) patients with and without tardive dyskinesia showed similarly poor cognitive function; however, the substantially greater use of anticholinergics reported in the *non*dyskinetic group may have compromised this comparison.

Most body regions are presumed to be potentially at risk for tardive dyskinesia, but some weight of evidence (Waddington, 1989) now suggests that involuntary orofacial (i.e., buccal–lingual–masticatory) movements may constitute a "core" syndrome that is pathophysiologically distinct from involuntary movements with other, primarily limb/trunkal topographies. In the present context, two studies (Waddington, Youssef, Dolphin, & Kinsella, 1987; DeWolfe, Ryan, & Wolf, 1988) have indicated the association between tardive dyskinesia and cognitive dysfunction in schizophrenia to be most evident for, if not exclusive to, involuntary movements with an orofacial topography; thus, the consideration of involuntary movements of other body areas in the diagnosis of tardive dyskinesia may obscure any specific association with those of the orofacial region. There is some evidence that the association may be more robust in relation to persistent rather than to transient dyskinesia (Struve & Wilner, 1983).

EXEMPLIFICATION OF THE ASSOCIATION

The following study sought to clarify further the nature of any such association between cognitive dysfunction and tardive dyskinesia in schizophrenia, and illustrates some of the attendant problems of analysis and interpretation in relation to potential confounds discussed above.

Subjects and Procedures

Seventy-five unselected outpatients attending the depot neuroleptic clinic of Cluain Mhuire Family Centre, Co. Dublin, were evaluated using the Abnormal Involuntary Movement Scale (AIMS; National Institute of Mental Health, 1976). Of these, 64 were subsequently found to satisfy DSM-III criteria (American Psychiatric Association, 1980) for schizophrenia on the basis of casenote review and, where necessary, clinical interview (O'Callaghan, Larkin, Kinsella, & Waddington, 1990); it is to these 64 patients (37 male, 27 female; mean age 37.7 ± 12.3 [*SD*], range 20–68 years) that all further discussion relates.

Case records were reviewed to obtain the following additional demographic and clinical information: age at onset of illness, in terms of first contact with a psychiatric service; duration of illness; duration of neuroleptic treatment; current neuroleptic dose in chlorpromazine (CPZ) equivalents (Davis, 1976); duration of anticholinergic treatment; presence or absence of current exposure to anticholinergics; number of courses of electroconvulsive therapy (ECT); presence or absence of history of abuse of alcohol; educational attainment (1 = first level, left school before or at age 12; 2 = second level, left school before or at age 17; 3 = third level, attended University or College); married or single [divorce is constitutionally prohibited in Ireland]; presence or absence of a history of unemployment for >1 year; presence or absence of a history of premorbid signs. Cognitive function was evaluated as the time in seconds taken to complete Trail Making Tests A and B from the Halstead–Reitan battery, two visual scanning, visuomotor coordination, and (Test B) cognitive flexibility tasks sensitive to general organic brain dysfunction (Reitan, 1958); one patient was unable to complete this assessment.

Univariate comparisons on the above measures were effected using Student's *t* test of the Fisher exact probability test (two-tailed). These variables were then examined for their relationship to tardive dyskinesia measures using stepwise multiple logistic regression and stepwise multiple linear regression procedures.

Results

There were 24 of the 64 patients (37.5%) who satisfied the criteria of Schooler and Kane (1982) for tardive dyskinesia when applied solely to the orofacial area, i.e., on the basis of scores over items 1–4 of the AIMS.

As indicated in Table 2, univariate comparisons indicated patients with and without tardive orofacial dyskinesia not to be distinguished by sex distribution, current neuroleptic dosage or exposure to anticholinergics, abuse of alcohol, educational level, marital status, unemployment history, or premorbid signs. However, those with such dyskinesia were characterized by greater age, age at onset of illness, duration of illness, duration of neuroleptic treatment, duration of anticholinergic treatment, and number of courses of ECT, and by poorer cognitive function in terms of each of Trail Making Tests A and B.

These data were entered into stepwise multiple logistic regression analysis to construct a hierarchy of those variables having independent associations with the binary measure of presence or absence of tardive orofacial dyskinesia. As shown in Table 3, the goodness-of-fit of the final logistic regression model was satisfactory, and it indicated poor performance on Trail Making Test B to be the primary variable associated with the presence of tardive orofacial dyskinesia; only duration of illness tended to show any association with the presence of such movement disorder independent of intercorrelation with the primary variable.

Severity of tardive orofacial dyskinesia was defined as the total score summed over the first four items of the AIMS. These data were entered into stepwise multiple linear regression analysis to construct a hierarchy

TABLE 2
Characteristics of Patients with and without Tardive Orofacial Dyskinesia

Variable	Tardive dyskinesia	
	Absent	Present
Number (male and female)	40(25 M, 15 F)	24(12 M, 12 F)
Age (years)	32.3 ± 8.6	46.5 ± 12.6*
Age at onset of illness (years)	23.0 ± 5.9	27.6 ± 5.3*
Duration of illness (years)	9.2 ± 5.6	18.8 ± 10.3*
Duration of neuroleptics (years)	6.7 ± 4.6	12.2 ± 6.0*
Current neuroleptic dose (mg CPZ)	487 ± 339	496 ± 395
Duration of anticholinergics (years)	4.1 ± 3.9	7.0 ± 4.0*
Current anticholinergics	24/40	21/24
Courses of ECT	0.8 ± 1.0	3.2 ± 3.9*
Abuse of alcohol	8/40	6/24
Educational level (stage attained)	2.0 ± 0.7	1.6 ± 1.0
Married	8/40	7/24
Unemployed > 1 year	26/40	12/24
Premorbid signs	11/40	9/24
Trail Making Test A (seconds)	47.7 ± 15.8	72.3 ± 29.1*
Train Making Test B (seconds)	103.1 ± 41.7	212.1 ± 108.2*

Note. Data are means ± *SD* or prevalences.
* $p < .01$, Student's *t* test; *t* values > 2.66; $df = 62$ except Trail Making Tests where $df = 61$ (see text).

TABLE 3
Hierarchy of Variables Related by Stepwise Logistic Regression Analysis to the Presence of Tardive Orofacial Dyskinesia

Variable	β	*SE*β	β/*SE*β	χ^2	*p*
Trail Making Test B	0.23×10^{-1}	0.73×10^{-2}	3.21	31.21	<.001
Duration of illness	0.93×10^{-1}	0.50×10^{-1}	1.86	3.69	.055

Note. Goodness-of-fit tests: Hosmer, $\chi^2 = 6.97$, $p = .54$; Brown, $\chi^2 = 0.49$, $p = .78$.

of those variables having independent associations with this ordinal measure. As shown in Table 4, the goodness-of-fit of the final linear regression model was satisfactory, and indicated poor performance on Trail Making Tests A and B to be associated independently with increasing severity of tardive orofacial dyskinesia; no other variable showed any independent association with the severity of such movement disorder.

Discussion

In the present population, univariate comparisons indicated patients with tardive orofacial dyskinesia to be older and to have been ill for a longer period than those who remained unaffected. Age and duration of illness are highly intercorrelated in chronic schizophrenia. Thus, among several potential causal explanations, the longer duration of exposure to neuroleptics and to anticholinergics in dyskinetic patients, and receipt of more courses of ECT, may reflect their greater age/duration of illness rather than indicate any direct role in the initiation of their movement disorder. The apparent relationship between dyskinesia and older age at onset of illness, as distinct from chronological age, may potentially reflect, at least in part, some greater difficulty in specifying the onset of psychosis in more elderly patients; however, associations between tardive dyskinesia and age at onset of illness have been reported previously, and are open to other interpretations (see Waddington, 1989).

The poorer cognitive function of patients with vs. those without tardive orofacial dyskinesia is thus only one of several measures distinguishing such patients on univariate comparison; indeed, it could be argued that

TABLE 4
Hierarchy of Variables Related by Stepwise Linear Regression Analysis to the Severity of Tardive Orofacial Dyskinesia

Variable	β	*SE*β	β/*SE*β	*p*	R^2
Trail Making Test A	0.10	0.31×10^{-1}	3.18	<.005	27.7
Trail Making Test B	0.25×10^{-1}	0.85×10^{-2}	2.95	<.01	35.8
Constant	1.80	—	—	—	—

the greater cognitive impairment in dyskinetic patients might itself be an epiphenomenon of their greater age/duration of illness. However, on multivariate analysis, stepwise logistic regression identified poor cognitive function as the primary factor distinguishing patients with from those without tardive orofacial dyskinesia. This relationship was most evident in terms of poor performance on Trail Making Test B, which requires motor acts identical to those necessary for Test A but places considerable additional demand on cognitive flexibility; such data argue for primacy of cognitive over any performance deficit. No other variables, including those which distinguished dyskinetic from nondyskinetic patients on univariate comparison, were so identified as having any significant *independent* association with the presence of such movement disorder. The reliable increase in the prevalence of tardive dyskinesia with older age/duration of illness might reflect certain poorly defined patterns of cerebral change, and the present results indicate cognitive impairment to be the primary correlate of such changes. It could therefore be argued that increasing age/duration of illness may be simply one factor making it more likely that the cerebral dysfunction reflected in cognitive impairment will be present. Among subgroups of patients who were of indistinguishable age, poor cognitive function on Trail Making Test B was still found to be the primary variable characterizing the dyskinetic group (O'Callaghan et al., 1990). These issues are fundamental to subsequent discussion.

NATURE OF THE ASSOCIATION BETWEEN COGNITIVE DYSFUNCTION AND TARDIVE DYSKINESIA

Generalizability across Diagnostic Groups

Were such an association to have any general relevance to tardive dyskinesia, one would expect to detect it in other diagnostic groups for which neuroleptics are prescribed and in which this movement disorder has been documented. Though the great majority of studies have involved patients with schizophrenia, similar findings have been reported in neuroleptic-treated patients with affective illnesses, particularly bipolar affective disorder (Wolf, Ryan & Mosnaim, 1983; Waddington & Youssef, 1988a; Waddington, Brown, O'Neill, McKeon, & Kinsella, 1989a; Hunt & Silverstone, 1991; for equivocal findings, see DeWolfe et al., 1988) and in a mixed population of schizophrenic and affective patients where the association appeared unrelated to diagnosis (Wade, Taylor, Kasprisin, Rosenberg, & Fiducia, 1987; Wade, Lehmann, Hart, Linden, Novak, & Hamer, 1989); similar findings have also been reported in neuroleptic-treated patients with mental handicap (Gualtieri, Schroeder, Hicks, & Quade, 1986; Youssef & Waddington, 1988; but see Richardson, Haugland, Pass, & Craig, 1986). However, systematic studies in such popula-

tions with nonschizophrenic diagnoses are as yet relatively few, and further work to clarify this matter is clearly necessary.

Organic Vulnerability to Tardive Dyskinesia?

Perhaps the most critical issues are whether apparently greater cognitive impairment in schizophrenic patients with tardive dyskinesia implies an excess of organic brain changes, and whether these might be expected to have arisen before initiation of neuroleptic therapy; if so, they might constitute a prominent preexisting vulnerability factor for this movement disorder on subsequent neuroleptic treatment. The vast majority of studies are cross sectional in nature, comparing populations of patients with vs. without tardive dyskinesia, and little is available in the way of prospective or longitudinal data necessary to address the matter satisfactorily. It has been suggested (Jeste, Grebb, & Wyatt, 1985) that the cognitive impairments associated with tardive dyskinesia resemble those of subcortical dementia as seen in certain neurological disorders, particularly subcortical frontal lobe disease.

A first approach is to clarify whether schizophrenic patients with tardive dyskinesia show an overrepresentation of other putative indices or direct evidence of organicity in cross-sectional studies. The literature on neurological soft signs, EEG abnormalities and structural brain pathology on X-ray computed tomography (CT) is provocative but not conclusive on the matter, with positive associations with tardive dyskinesia tending to be perhaps somewhat more common in older, chronically ill patients with the more prominent and persistent orofacial dyskinesia (Waddington, 1989). Very recent findings are similarly inconclusive. We have not been able to distinguish schizophrenic outpatients with tardive dyskinesia from similar patients without such movement disorder in terms of cerebral ventricular size, signal hyperintensities, or cortical atrophy on magnetic resonance imaging (MRI; Waddington, O'Callaghan, Larkin, Redmond, Stack, & Ennis, 1990b); however, even MRI will be insensitive to subtle structural brain pathology or to brain tissue that is functionally impaired yet structurally intact. Among older, chronically ill schizophrenic inpatients, those with persistent, tardive orofacial dyskinesia did appear particularly characterized by an excess of neurological soft signs and increased ventricle–brain ratio on CT (Waddington, Youssef, King, & Cooper, 1989b; King, Wilson, Cooper, & Waddington, 1991).

Regarding the timing and significance of cognitive dysfunction itself, Manschreck, Keuthen, Schneyer, Celada, Laughery, and Collins (1990) have reported a putative index of premorbid intellectual ability to be somewhat reduced in schizophrenic patients with tardive dyskinesia; while this might be consistent with some early, predisposing cognitive impairment, it may be confounded with current cognitive deficits that were evident on the same occasion. It has been reported by Wegner, Kane, Weinhold, Woerner, Kinon, and Lieberman (1985b), from the prospective study of a relatively young, heterogeneous population, that poor neuropsychological test performance among those initially without dyskinesia was associated with the subsequent emergence of such movement disorder a mean of 1.6 years later; however, this patient population carried primarily affective diagnoses, for which an association between cognitive dysfunction and tardive dyskinesia is less extensively studied, and indeed the relationship appeared to show some diagnostic specificity for affective disorders rather than schizophrenia. These two reports also have to be set against the studies considered previously which suggest that while schizophrenic patients with tardive dyskinesia may be more likely to show signs of organicity, such findings appear to be somewhat more common in older, chronically ill inpatients. Thus, the inconclusive nature of this literature leaves open the possibility of explanations other than organic vulnerability.

State Marker for Tardive Dyskinesia?

In a longitudinal study of older, chronically ill schizophrenic inpatients without tardive dyskinesia, poor initial cognitive function was not predictive of the subsequent emergence of such movement disorder on long-term follow-up; however, those patients who went on to develop tardive orofacial dyskinesia were distinguished by a selective deterioration in their cognitive function over the same time frame in which their movement disorder emerged, suggesting some close temporal relationship between these two phenomena (Waddington, Youssef, & Kinsella, 1990a). An unexpected finding in this study was the identification prospectively of a positive family history of major psychiatric disorder as a predictor of the emergence of tardive orofacial dyskinesia; a cross-sectional association between the presence of such movement disorder and a positive family history of schizophrenia was noted in a subset of the total group of 64 patients described above (O'Callaghan et al., 1990), and concordance for cognitive dysfunction and tardive orofacial dyskinesia in schizophrenia has been noted in multiply affected members of a large psychotic sibship (Waddington & Youssef, 1988b).

Such longitudinal data raise again the possibility that the association between cognitive dysfunction and tardive dyskinesia may reflect not organic vulnerability to but rather a state marker for this movement disorder. In these situations, cognitive dysfunction may be, at least in part, another manifestation, or epiphenomenon, of whatever pathophysiologi-

cal process(es) may underlie tardive dyskinesia. For example, while neuroleptics do not appear to exert any major, generalized effect on cognitive function (King, 1990; Cassens et al., 1990), long-term treatment with such drugs might, in some patients, be associated with the emergence not only of tardive dyskinesia but also of cognitive deterioration; the negative relationship between cognitive function and patient age noted in chronic schizophrenic inpatients with but not in those without tardive orofacial dyskinesia (Waddington et al., 1989b) would be consistent with a process of this type. Such a scheme would be a variant of the notion of "tardive dysmentia" or "tardive dementia," as previously reviewed by others (Goldberg, 1985; Myslobodsky, 1986) and reconsidered in recent studies of tardive orofacial dyskinesia (DeWolfe et al., 1988; McClelland, Metcalfe, Kerr, Dutta, & Watson, 1991).

It must be emphasized that studies of these phenomena do not utilize diagnostic instruments, and hence they cannot distinguish per se between neuroleptic-associated tardive dyskinesia and similar involuntary movement disorder(s) with other origins. Though long-term neuroleptic treatment is clearly associated with the emergence of tardive dyskinesia, there is increasing evidence (Waddington, 1989) that the baseline level/prevalence of involuntary movements unrelated to neuroleptic exposure may have been underestimated in a number of instances; thus neuroleptics may have some action to hasten the emergence of an inappropriate and overelaborated form of innate buccal–lingual–masticatory motor patterns that have an unappreciated likelihood of ultimately occurring spontaneously with cerebral dysfunction. If tardive dyskinesia can indeed be a neuroleptic-precipitated variant of a covert [or sometimes overt] disease-related predisposition to such movement disorder, is there any evidence that spontaneous dyskinesia may also be associated with cognitive dysfunction? There are few systematic studies on this issue, but compatible data have been reported in neuroleptic-naive patients with chronic schizophrenia (Owens & Johnstone, 1980; Waddington & Youssef, 1990), Alzheimer's disease (Molsa, Marttila, & Rinne, 1984; but see Bakchine, Lacomblez, Pallison, Laurent, & Derouesne, 1989), and mental handicap (Dinan & Golden, 1990).

Were such preliminary findings to be sustained, it would be further consistent with the notion (Waddington, 1989, 1990; Rogers, Karki, Bartlett, & Pocock, 1991) of neuroleptics as agents which, on long-term administration, interact with and ultimately disturb the cerebral substrates of various neuropsychiatric disorders. Further studies will be necessary to clarify the extent to which this might include a concurrent influence on cognitive as well as involuntary motor function, or an influence on systems whose predisposition to involuntary movement disorder is reflected in preexisting cognitive dysfunction.

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Factors Related to the Severity of Tardive Dyskinesia

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This study was undertaken to clarify factors associated with severity of tardive dyskinesia (TD). It was hypothesized that dopaminergic changes associated with neuroleptic medication may interact with unknown vulnerabilities contributing to the manifestation of TD. Fifty-four psychiatric patients residing on the acute and intermediate care wards of a Veterans Administration hospital participated. Thirty schizophrenic and 24 manic patients, under 60 years of age, were assessed for TD using the Abnormal Involuntary Movement Scale. Cognitive tests were used to form verbal and nonverbal composite indices. The results of multiple regression analyses revealed a modest linear relationship between TD and nonverbal function ($p < .03$) after controlling for duration of hospitalization, years of illness, motor speed, and age. This relationship was noted for both manic and schizophrenic patients. The results of this study suggest that nonverbal dysfunction is related to severity of TD. © 1993 Academic Press, Inc.

INTRODUCTION

Reports of a neuroleptic-induced syndrome characterized by involuntary abnormal facial movements appeared in the late 1950s. Uhrbrand and Faurbye (1960) first applied the term "tardive dyskinesia" (TD), implying an often delayed reaction caused by neuroleptic therapy. By 1974, TD was considered to be a well-defined neurologic entity and a major iatrogenic disease (Baldessarini, 1974). The reported prevalence of TD in hospitalized psychiatric patients varies greatly, from 5 to 40%, with a mean of 25% (Baldessarini, 1974; Fann, Davis, & Janowsky, 1972; Yassa, Nair, Iskandar, & Schwartz, 1990). The wide variation may be explained by differing patient selection procedures and methods used to define the disorder.

Many attempts have been made to clarify variables associated with TD severity. Although it is clear that TD represents an iatrogenic result of neuroleptic administration, to date there is no clear evidence that TD is

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