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Tardive Dyskinesia and Cognitive Impairment

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Introduction

Several studies (Famuyiwa et al. 1979; Struve and Wilner 1983; Wolf et al. 1983; Myslobodsky et al. 1985) point to an association between tardive dyskinesia and cognitive functioning, although these findings are not always replicated (Pryce and Edwards 1966; Edwards 1970; Donnelly and Jeste 1981). The present study was conducted to further evaluate the relationship between cognitive function and tardive dyskinesia. Given the notion that Parkinson's and Huntington's diseases might provide a neuropsychological, as well as a biochemical, model for tardive dyskinesia (Myslobodsky et al. 1985), tasks were selected that reveal cognitive impairment in these disorders.

Methods

Subjects

We studied 54 male psychiatric patients receiving neuroleptics and residing on the short-term or intermediate care wards of a public hospital. In order to separate the cognitive impairment due to the psychiatric illness from that associated with tardive dyskinesia, we compared schizophrenics and manics. The criteria for schizophrenia were those of Taylor and Abrams (1978) and for mania were those of Feighner et al. (1972). The sample consisted of 30 schizophrenics and 24 manics. Mean age for the schizophrenics was 44.9 years (SD = 12.30) and for the manics 47.12 years (SD = 14.50). Except for years of education (schizophrenics 11.60 ± 3.23; for manics 13.29 ± 2.88; $F = 4.015$, df $= 1, p < 0.05$), the two groups did not differ significantly on years of illness (schizophrenics 21.10 ± 11.69, for manics 16.18 ± 2.88), years of hospitalization (schizophrenics 11.97 ± 10.11, for manics 10.51 ± 12.04), or severity of tardive dyskinesia (schizophrenics 6.00 ± 4.92; for manics 5.12 ± 5.35).

Cognitive Battery

The battery consisted of tasks that have been shown (Butters et al. 1979; Pirozzolo et al. 1982) to be sensitive to cognitive changes associated with Huntington's and Parkinson's disease. The battery included: (1) selected Wechsler Adult Intelligence Scale subtests (information, arithmetic, digit span, picture completion, picture arrangement) (Wechsler 1945); (2) selected portions of the Wechsler Memory Scale (logical memory, visual reproduction, paired associate learning) (Wechsler 1945); (3) Serial 7's of the Mini-Mental State Exam (Folstein et al. 1975); (4) the Verbal Fluency Test of Butters et al.

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(1979); and (5) Russell's (1975) Scales of Verbal and Figural Long-Term Memory (requiring the subject to recall the original verbal and figural material a half hour after presentation).

The Assessment of Tardive Dyskinesia

Tardive dyskinesia was assessed as a continuous variable using the total score from a modificiation (Smith et al. 1979) of the Abnormal Involuntary Movement Scale (AIMS) (Guy 1976).

Procedure

After the psychiatric interview, each subject was rated for severity of tardive dyskinesia. After the AIMS was administered, demographic data were recorded from the patient's medical chart. A second investigator, blind to diagnosis and the AIMS rating, administered the cognitive test battery to each subject.

Results

To assess the relationship between tardive dyskinesia and cognitive impairment, we statistically accounted for the effects of subject age, years of education completed, diagnosis, length of illness, and duration of hospitalization by a hierarchical multiple regression that permits partitioning of the total variance uniquely accounted for by each predictor variable (Cohen and Cohen 1975). Table 1 displays the results of the regression analysis. Tardive dyskinesia provided moderate and significant prediction of cognitive performance after all other variables were controlled (change in $R^2 = 0.09$, $p < 0.02$). Besides age, no other variables accounted for a significant proportion of the variance in cognition. Given the possibility that preexisting cortical abnormality predisposes an individual to tardive dyskinesia (e.g., the association between tardive dyskinesia and cognition might differ for schizophrenics and manics), we included interaction terms in the regression analysis, but none of these terms accounted for a significant amount of variance in cognition after main effects were considered. Using an additional hierarchical regression analysis, we examined the variables tardive dyskinesia severity and cognitive performance for a curvilinear relationship. None of the curvilinear models accounted for significantly more variance than the restricted linear model.

Table 1. Hierarchical Multiple Regression Predicting Cognitive Impairment in Schizophrenic and Manic Patients (n = 54)

Variable	R^2 change	F^a	R^2	F^b
Age	0.147	8.969[d]	0.147	8.969[d]
Education	0.020	1.273	0.167	5.145[d]
Diagnosis	0.001	0.089	0.169	3.398[c]
Years of illness	0.007	0.461	0.177	2.636
Years of hospitalization	0.009	0.535	0.186	2.196
Severity of tardive dyskinesia	0.091	5.939[c]	0.277	3.008[c]

[a]This F represents the unique prediction of each variable after the preceding terms are removed.
[b]This F represents the test of significance of the total regression equation for all variables included in the equation up to that step.
[c]$p < 0.05$.
[d]$p < 0.01$.

We also assessed the extent to which cognitive performance was due to motor disturbance under timed conditions. To do this, we determined a global cognitive performance score for each subject by summing their standard scores on the eight untimed tests with the "limits-testing" scores on the four timed subtests (including points attained after the time limit for task discontinuance). A regression analysis was performed to determine whether or not tardive dyskinesia could predict cognitive performance when the cognitive measures did not contain a timed motor component. Tardive dyskinesia accounted for 8% of the variance in the global cognitive test score (change in $R = 0.08$, $p < 0.03$). Thus, the observed relationship between tardive dyskinesia and cognition is not due simply to motor slowing.

Discussion

These results reveal a modest, but statistically significant, relationship between tardive dyskinesia and cognitive functioning in psychiatric patients, even after accounting for the effect of illness variables and motor speed. These findings are consistent with those of Famuyiwa et al. (1979), lending support to the hypothesis that tardive dyskinesia may represent the extent or severity of a chronic neuroleptic-induced neurotoxic process. Furthermore, the relationship appears to be linear: individuals with severe forms of the disorder are most impaired cognitively. This is similar to the relationship observed by Pirozzolo et al. (1982) in Parkinson's disease patients. Clarification of the relationship between tardive dyskinesia and cognition is critical, as our data and those of others suggest that a relationship may exist that contributes to unnecessary morbidity.

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