Comparison Between the Effects of Atypical and Traditional Antipsychotics on Work Status for Clients in a Psychiatric Rehabilitation Program

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Background: Although many studies have compared the impact of atypical antipsychotics with that of traditional antipsychotics on psychiatric symptoms, few have compared the impact on work status, especially in the context of best-practices psychiatric rehabilitation.

Method: A cross-sectional design examined symptom and employment status for 82 clients with DSM-IV schizophrenia-spectrum disorders who had attended a psychiatric rehabilitation program for a mean of 5 years. Using chart review and client interviews, we examined the relationship between type of antipsychotic prescribed and symptom and work status in 59 clients prescribed an atypical antipsychotic (olanzapine or risperidone) for a mean of 20 months and 23 clients prescribed a traditional antipsychotic for a mean of 75 months. Measures included the Positive and Negative Syndrome Scale and 2 work status measures: an 8-point employment status scale (the Work Placement Scale) and percentage of clients working in independent employment.

Results: The atypical group had significantly fewer symptoms of cognitive impairment and hostility/excitement than the traditional group ($p < .05$). However, self-reported adverse events were similar in the 2 medication groups, and the 2 groups did not differ significantly on work status. Less severe negative, cognitive, and hostility/excitement symptoms were associated with more independent employment status.

Conclusion: For long-term clients in a psychiatric rehabilitation program, type of medication prescribed was associated with better symptom control but not better work status. The association between symptoms and work status, however, may suggest an indirect link favoring atypical antipsychotics for achieving paid employment.

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Atypical antipsychotic medications, a term commonly used to describe a group of newer antipsychotic agents developed with the intent of achieving high efficacy accompanied by a low extrapyramidal symptom profile within the therapeutic range to treat psychosis in schizophrenia,[1] are rapidly replacing traditional antipsychotics in the treatment of schizophrenia in the United States. A recent survey found that about half of all patients with schizophrenia were being prescribed olanzapine or risperidone, medications not even available a decade ago.[2,3] Although traditional antipsychotics have shown value in controlling the positive symptoms of schizophrenia and reducing relapse rates,[4,5] they are not effective in a significant minority of patients.[6] Moreover, their impact on negative symptoms has been negligible.[5,7] As is widely known, the most serious limitation in the use of traditional antipsychotic agents is that many individuals develop extrapyramidal symptoms (EPS).[8] Lack of medication efficacy and the development of EPS are major factors in medication noncompliance, a substantial barrier in the effective treatment of schizophrenia.[9–12]

As reflected in recent practice guidelines,[13,14] many experts have concluded that atypical antipsychotic medications generally are clinically superior to traditional antipsychotics. While EPS, symptom reduction, and relapse vary between olanzapine and risperidone, both olanzapine and

risperidone are superior to haloperidol in terms of risk of EPS.[15–18] Olanzapine has demonstrated superiority to haloperidol in reducing positive symptoms, and both olanzapine and risperidone may be more effective than haloperidol in treating negative symptoms.[8,17–22] Olanzapine also may be more effective than haloperidol in reducing depressive symptoms.[21] Finally, individuals with schizophrenia who are treated with atypical agents may have better cognitive functioning than do those receiving traditional antipsychotic agents.[23–25]

WORK STATUS WITH ANTIPSYCHOTIC TREATMENT

Lehman[26] has distinguished between proximal and distal outcomes of antipsychotic agents. *Proximal* outcomes refer to those that may be closely associated with the medications (e.g., psychiatric symptoms), whereas *distal* outcomes refer to consequences that, albeit critical, are less directly linked to an antipsychotic treatment (e.g., quality of life).

More information is needed regarding the impact of atypicals on a variety of important distal outcomes, including vocational functioning.[26,27] The hope has been that newer antipsychotics, through greater control of certain symptoms and improved cognitive functioning, would result in a "cascade" effect in which these better proximal outcomes lead to better distal outcomes.[26,28] The hypothesis that atypical antipsychotics improve vocational functioning is bolstered by studies suggesting an association between improved work outcomes and both control of negative symptoms[29–35] and better cognitive functioning.[24,35–39]

To date, only a few studies have examined the impact of atypicals on distal outcomes. Some suggest improved quality of life or general role functioning with the use of atypicals, but do not specifically address work outcomes.[40–44] In the few studies specifically examining work outcomes, substantial improvement has been found after clients were treated with clozapine[45,46] or with olanzapine.[47] A cross-sectional study found that clients receiving clozapine, risperidone, or olanzapine had a higher employment rate than did those receiving a traditional antipsychotic.[48] The most rigorous of these evaluations of the impact of an atypical agent on employment rates is a double-blind randomized controlled trial comparing 520 patients receiving olanzapine with 258 receiving haloperidol.[49] This study found that a significantly higher percentage of olanzapine-treated patients were competitively employed at 1 year (15% vs. 5%). However, the employment rate for the group treated with olanzapine is similar to the base rate of 15% or less found in many surveys.[50] Therefore, despite the obvious strengths of this study, it also exemplifies one limitation in most current research on the impact of medications on work functioning: it was not designed to examine antipsychotic treatment within the context of intensive vocational rehabilitation programming. Studies have consistently found low rates of community employment for clients with schizophrenia in the absence of psychosocial interventions and professional support.[51] Consequently, provision of effective medications is in itself unlikely to lead to dramatic increases in work outcomes.

MEDICATION EFFECTS IN THE CONTEXT OF VOCATIONAL REHABILITATION

The last decade has yielded significant progress in identifying vocational rehabilitation program models effective in helping people with severe mental illness achieve better work outcomes.[51–55] A controlled study[52] has shown that people with schizophrenia can work if they receive adequate support and that they can achieve employment rates above the 15% base rates reported in many surveys. Unfortunately, studies of exemplary vocational programming have focused narrowly on psychosocial interventions while neglecting the assessment of medication effects. Most observers agree that medications in combination with best practices in psychiatric rehabilitation lead to greater improvements in role functioning than do either intervention type in the absence of the other.[56–59] Unfortunately, to date, few studies have examined this hypothesis directly.[60] The current study was based on the hypothesis that best-practices vocational rehabilitation provides the appropriate treatment environment in which to examine the impact of medications.

STUDY PURPOSES

We conducted a naturalistic, cross-sectional study of long-term clients in an exemplary psychiatric rehabilitation program. Two treatment groups were compared; 1 was prescribed an atypical antipsychotic (either olanzapine or risperidone) and the other was prescribed 1 of several possible traditional antipsychotic agents. We tested the following hypotheses: (1) those in the atypical group would have better psychiatric symptom control and a reduction in self-reported adverse events compared with those in the traditional group, (2) better control of symptoms would be associated with better work status, (3) a less severe experience with adverse events would be associated with better work status, and (4) the atypical group would have better work status than would the traditional group.

METHOD

Setting

The study was conducted at 2 vocationally oriented day programs operated by Thresholds, a psychiatric rehabilitation agency in Chicago, Ill., for persons with severe

mental illness. Initially developed in the 1950s as a psychosocial clubhouse program, Thresholds has developed a comprehensive set of services addressing employment, independent living, socialization, academic achievement, and avoidance of hospitalization.[61] Vocational placements are offered in a stepwise manner with an ultimate goal of paid employment in an integrated setting.[51,61,62] Through agreements with businesses, the agency provides clients with an array of possible paid placements, commensurate with their current capabilities and preferences. Options include group and individual placements arranged between Thresholds and employers, enclaves, agency-run businesses, supported employment, and independent jobs. All clients entering the vocational program initially attend prevocational work crews. However, there are no time requirements for any specific step in the continuum, nor are clients required to complete any specific placement option after the prevocational work crew. Although the vocational program is conceptualized as a stepwise continuum in which clients generally progress during their tenure at Thresholds from an initial placement in an unpaid work crew through intermediate protected work experiences toward the goal of independent employment in their own competitive employment position, the program placement process is very flexible. The net result for most clients is nonlinear progression, punctuated by periods of progress, setbacks, and plateaus.[53]

Sampling and Recruitment

Retrospective chart reviews and client interviews were conducted in 1998 to test the study hypotheses.[63] Eligibility criteria were as follows: (1) age of 18 to 65 years; (2) chart diagnosis of DSM-IV schizophrenia, schizoaffective disorder, or schizophreniform disorder; (3) admission to the agency at least 6 months prior to participation in the study (because agency statistics suggest that prior to 6 months' tenure in the program most clients have not had an opportunity to obtain paid employment); (4) attendance at 1 of 2 Thresholds day programs (Thresholds North and Thresholds South); (5) currently prescribed olanzapine, risperidone, or a traditional antipsychotic (but no 2 in combination); (6) not currently prescribed clozapine (to avoid the possibility of a biasing effect from oversampling treatment-resistant patients)[64]; (7) prescribed antipsychotic medication for at least the prior 6 months; and (8) informed consent given.

Potential study participants were identified through a chart review of medications and diagnosis. A research assistant approached eligible clients, explained the study, and determined willingness to participate. Clients who agreed then signed an informed consent statement and scheduled an initial interview, during which information about employment history, medication history, current medications, and perceived adverse events was obtained. Subsequently, clients completed a clinical interview, which included the assessment of current psychiatric symptoms. Clients were paid for completing each interview.

Originally, we planned quota sampling with equal Ns (approximately 30) for each of 3 medication groups: olanzapine, risperidone, and traditional antipsychotics. Within the time frame for the study, we obtained 33, 26, and 23 clients, respectively, in the olanzapine, risperidone, and traditional antipsychotic groups. The reduced numbers for the risperidone and traditional groups mainly reflected the use patterns at the study sites. Medications prescribed in the traditional group included haloperidol, fluphenazine, thiothixene, chlorpromazine, thioridazine, and trifluoperazine.

The olanzapine and risperidone clients differed on only 1 of the 13 background variables examined. Clients treated with risperidone had a significantly later mean age at onset (26.3 ± 10.3 years) than those treated with olanzapine (20.7 ± 6.1 years; $t = 2.44$, $df = 57$, $p < .05$). Because the olanzapine and risperidone groups were very similar on background and outcome variables, they were collapsed into a single "atypical" group to increase statistical power.

Data Sources

Background information. Through review of client charts, we obtained information relating to a variety of demographic, illness and treatment history, and clinical status variables. Demographic variables were age, education level, gender, race/ethnicity, and marital status. Other background variables, relating to disease and treatment history, included program location (North or South location), tenure at Thresholds, length of time on treatment with current antipsychotic medication, and use of an anticholinergic medication (used to treat or prevent EPS). Finally, clinical variables examined included primary diagnosis (schizophrenia, schizoaffective, or schizophreniform disorder), age at first psychiatric hospitalization, number of lifetime psychiatric hospitalizations, and Global Assessment of Functioning (GAF)[65] rating.

Psychiatric symptoms. The Positive and Negative Syndrome Scale (PANSS)[66] was used to measure symptom severity. The PANSS is a widely used semistructured interview that uses standardized ratings of symptoms. Three clinical psychology graduate students with a minimum of 4 hours of supervised training in PANSS symptom interviewing conducted these interviews. A clinical psychologist with extensive experience administering the PANSS supervised the interviewers.

Bell et al.[67] identified 5 PANSS subscales: The positive and negative factors (6 and 8 items, respectively) assess the positive (hallucinations and delusions) and negative (withdrawal, motor retardation, speech production) symptoms of schizophrenia. The emotional discomfort factor (4 items) describes the affective state, including the severity of depression and anxiety. The hostility/

excitement factor (4 items) includes hostility, excitement, uncooperativeness, and poor impulse control, while the cognitive factor (7 items) centers on abstract thinking, attention, and insight. In the current study, the internal consistency coefficients (Cronbach α) were 0.74 for the positive scale, 0.73 for the negative scale, 0.64 for the cognitive scale, 0.67 for the emotional discomfort scale, and 0.49 for the hostility/excitement scale.

Adverse events. For this study, we devised a 10-item checklist of adverse events sometimes reported during treatment with antipsychotics (drowsiness, weight gain, sexual problems, insomnia, restlessness, stiffness, dry mouth, drooling, blurred vision, constipation). For each item, clients were asked if they had ever experienced it, and if so, whether it had changed for the better, for the worse, or not changed since beginning their most recent medication. Responses of "unchanged" or "worsened" were categorized as a perceived adverse event.

Work status measures. Employment data were obtained from a computerized database maintained at Thresholds. Information was checked for accuracy with each client, with his or her case manager, and with vocational program staff. Two related indicators were used to assess work status.

The Work Placement Scale (WPS) was adapted from the placement reports used by Thresholds staff to track client progress[68] and from the vocational measurement recommended by the International Association of Psychosocial Rehabilitation Services (IAPSRS) Outcome Toolkit.[69] It consists of 8 levels of employment, using a gradient that reflects the goals of the vocational program of the agency. These levels are (1) unemployed, (2) prevocational training, (3) volunteer work, (4) sheltered workshop, (5) agency-run business, (6) agency-contracted group placement, (7) agency-contracted individual placement, and (8) competitive employment. Agency-contracted placements are jobs in community settings paying at least minimum wage that are secured through agreements between Thresholds and employers. Competitive employment refers to community jobs paying at least minimum wage that any person can apply for. Competitive jobs do not involve formal agreements between Thresholds and employers.

The second and related indicator of work outcome was the percentage of clients achieving integrated employment, defined as working in an individual agency-contracted placement or in competitive employment. These top 2 levels in the WPS represent attainment of independent employment in integrated work settings (i.e., coworkers are not Thresholds clients and supervisors are not Thresholds employees).

Data Analyses

Distributional properties of the outcome measures and measures of time on medications and tenure at Thresholds were examined for outliers and skew. When tests for normality and homogeneity of variance were significant (indicating differing distributions), the separate error variance version of the t test was used. For all analyses comparing medication groups, independent t tests (2-tailed) were used for continuous variables and chi-square tests were used for categorical variables for all analyses. For analyses involving t tests, we also calculated effect sizes, using the d statistic.[70]

Because some client background variables have sometimes been shown to be significantly related to work outcomes,[54] we compared the 2 medication groups on background variables to help identify potential confounds. When significant differences were found, the relevant variables were also examined for their associations with employment outcome.

The analyses involved several steps. The test of hypothesis 1 consisted of t tests between the 2 treatment groups on clinical outcomes (i.e., psychiatric symptoms and adverse events). Hypotheses 2 and 3 were tested through correlations between these clinical variables and work status. Finally, hypothesis 4 was tested by comparing the 2 defined treatment groups directly on work status.

RESULTS

Comparability of Medication Treatment Groups

In addition to the 82 clients who agreed to participate in the study, 19 clients declined to participate. The percentage of clients who refused did not differ significantly between the 2 medication treatment groups (14% [10/69] for the atypical group and 28% [9/32] for the traditional group), $\chi^2 = 2.66$, df = 1, N = 19, NS. Additionally, those who declined to participate did not differ significantly from study participants in age, gender, marital status, race/ethnicity, level of education, GAF score, diagnosis, lifetime psychiatric hospitalizations, and age at first hospitalization.

As shown in Table 1, the atypical and traditional antipsychotic treatment groups did not significantly differ with respect to 11 of the 13 background characteristics examined, suggesting comparability between the 2 medication groups. The groups differed on amount of time on antipsychotic medication and percentage of clients prescribed an anticholinergic medication.

Those in the atypical group had been prescribed their current medication for a much shorter period of time (mean = 20.0 ± 12.7 months, minimum = 6 months) than had those in the traditional group (mean = 75.2 ± 62.4 months, minimum = 10 months), as shown in Table 1. However, no relationship was found between symptoms and amount of time on treatment with medication within either the atypical or the traditional medication group. With 1 exception, time on treatment with medication was also not correlated with adverse events. Perceived problems with weight gain were associated with recency of

Table 1. Sample Characteristics[a]

Characteristic	Total Sample (N = 82)	Atypical (N = 59)	Traditional (N = 23)	Test of Significance
Age, y	40.8 (8.6)	41.5 (9.0)	39.1 (7.6)	t = 1.15, df = 80
Education, y	12.2 (2.7)	12.3 (2.4)	12.2 (2.0)	t = 0.07, df = 80
Gender, N (%)				χ^2 = 0.82, df = 1
Male	47 (57)	27 (46)	15 (65)	
Female	35 (43)	32 (54)	8 (35)	
Ethnicity, N (%)				χ^2 = 2.91, df = 2
White	26 (32)	20 (34)	6 (26)	
African American	55 (67)	39 (66)	16 (70)	
Hispanic	1 (1)	0 (0)	1 (4)	
Marital status, N (%)				χ^2 = 2.10, df = 4
Single	68 (83)	50 (85)	18 (78)	
Married	3 (4)	2 (3)	1 (4)	
Divorced	9 (11)	5 (9)	4 (17)	
Separated	1 (1)	1 (1.5)	0 (0.0)	
Widowed	1 (1)	1 (1.5)	0 (0.0)	
Primary diagnosis, N (%)				χ^2 = 2.59, df = 1
Schizophrenia	57 (70)	38 (64)	19 (83)	
Schizoaffective disorder	25 (30)	21 (36)	4 (17)	
Age at first hospitalization/age at onset, y	22.7 (7.8)	23.2 (8.6)	21.4 (5.2)	t = 0.91, df = 80
No. of lifetime hospitalizations	8.9 (9.8)	8.6 (10.1)	9.4 (9.2)	t = 0.33, df = 80
GAF score	53.8 (9.8)	53.5 (9.4)	54.6 (10.9)	t = 0.45, df = 80
Thresholds program				χ^2 = 0.21, df = 1
North	22 (27)	15 (25)	7 (30)	
South	60 (73)	44 (75)	16 (70)	
Tenure at thresholds, mo	61.0 (54.5)	65.5 (56.1)	49.5 (49.4)	t = 1.19, df = 80
Time on treatment with medication, mo	35.5 (42.4)	20.0 (12.7)	75.2 (62.4)	t = 6.51,* df = 80
Anticholinergic medication, N (%)	20 (24)	7 (12)	13 (57)	χ^2 = 17.90,* df = 1

[a]Values shown as mean (SD) unless noted otherwise. Abbreviation: GAF = Global Assessment of Functioning.
*p < .01.

medication change for clients treated with atypical medications, but this was not the case for those treated with traditional medications. More time on treatment with medication was significantly related to a higher level of independent employment (WPS) for the traditional medication group (r = –0.49, p < .05), but no relationship was found for the atypical group (r = 0.00).

A significantly lower percentage of the atypical group compared with the traditional group had been prescribed an anticholinergic medication, as shown in Table 1. No differences in symptoms, adverse events, or work status were found within the atypical group for clients prescribed anticholinergic medication compared with those who were not. Within the traditional medication group, cognitive symptoms were significantly less severe for clients prescribed anticholinergic medication compared with those who were not (t = 2.84, df = 21, p < .05) but no association was found between anticholinergic medication and work status. Also, within the traditional medication group, clients prescribed an anticholinergic medication were more likely to report blurred vision.

Finally, we examined time at Thresholds (number of months from program admission to date of interview) as a possible confound in the analysis of correlates. Time at Thresholds was not related to work status, either in the total sample or within the 2 medication groups. Longer duration at Thresholds was correlated with less emotional discomfort both in the total sample (r = –0.26, p < .05) and in the atypical sample (r = –0.27, p < .05). Tenure at Thresholds was also associated with reduced restlessness in the total sample. Otherwise, time at Thresholds was not related to symptoms or adverse events.

Table 2. Comparisons Between Atypical and Traditional Antipsychotic Groups on the PANSS (N = 79)[a]

Scale	Atypical (N = 56) Mean	Atypical (N = 56) SD	Traditional (N = 23) Mean	Traditional (N = 23) SD	Effect Size
Positive	1.80	0.80	1.79	0.73	–.01
Negative	1.94	0.78	1.88	0.83	–.08
Cognitive	2.00	0.58*	2.42	0.92*	.60
Hostility/excitement	1.27	0.42*	1.58	0.76*	.57
Emotional discomfort	2.41	0.96	2.15	1.06	–.25

[a]N = 79 because 3 participants did not complete the PANSS interview. The PANSS ranges from 1 = absent to 7 = extreme.
Abbreviation: PANSS = Positive and Negative Syndrome Scale.
*p < .05.

Hypothesis 1: Differences Between Medication Treatment Groups on Psychiatric Symptoms and Adverse Events

As shown in Table 2, the atypical group had significantly lower ratings than did the traditional group on 2 of the 5 PANSS subscales, the hostility/excitement and cognitive scales. In both cases, the effect size was large, indicating a substantial treatment group difference. It

should be noted that clients in both treatment groups were rated as having low levels of symptoms.

With the exception of perceived weight gain, which was reported by 53% (N = 31) of clients taking atypicals and 22% (N = 5) of those taking traditional antipsychotics, the 2 medication groups did not differ on any of the client-reported adverse events, as shown in Table 3. The percentage of clients reporting weight gain did not differ statistically between the olanzapine group (61%; 20/33) and the risperidone group (42%; 11/26).

Hypotheses 2 and 3: Relationship of Psychiatric Symptoms and Adverse Events to Work Status

As shown in Table 4, 3 PANSS subscales were associated with 1 of the 2 employment measures (hypothesis 2). Lower ratings on the hostility/excitement scale were significantly associated with higher levels of independent employment as measured by the WPS. Additionally, within the total sample, clients working in integrated employment settings had significantly lower ratings on the negative and cognitive scales than did those who were not. Adverse events were not associated with work status.

Hypothesis 4: Differences Between Medication Treatment Groups on Work Status

As shown in Table 5, the medication treatment groups did not differ significantly with respect to either measure of work status.

Table 3. Perceived Adverse Events (N = 82)

	Atypical (N = 59)		Traditional (N = 23)		
Perceived Adverse Event	N	%	N	%	χ^2
Drowsiness	22	37	5	22	1.81
Weight gain	31	53	5	22	6.38*
Sexual problems	9	15	5	22	0.49
Insomnia	7	12	5	22	1.23
Restlessness	7	12	6	26	2.51
Stiffness	13	22	3	13	0.85
Dry mouth	19	32	9	39	0.35
Drooling	12	20	3	13	0.59
Blurred vision	11	19	8	35	2.42
Constipation	8	14	4	17	0.20

*p < .05.

Table 4. Relationship Between PANSS Scores and Work Status (N = 79)[a]

	WPS Score (N = 79)	Integrated Employment					
		Yes (N = 11)		No (N = 68)			
Scale	r	Mean	SD	Mean	SD	t	Effect Size
Positive	–0.07	1.79	0.81	1.79	0.78	0.00	.01
Negative	–0.20	1.52	0.31	1.99	0.83	3.44**	.60
Cognitive	–0.22	1.53	0.38	2.21	0.71	3.09**	1.00
Emotional discomfort	–0.17	2.14	0.98	2.36	0.99	0.70	.22
Hostility/excitement	–0.23*	1.14	0.30	1.40	0.58	1.46	.47

[a]N = 79 because 3 participants did not complete the PANSS interview.
Abbreviations: PANSS = Positive and Negative Syndrome Scale, WPS = Work Placement Scale.
*p < .05.
**p < .01.

Table 5. Work Placement Status for Medication Groups[a]

Work Placement Status	Atypical (N = 59)	Cumulative % Employed for Atypical	Traditional (N = 23)	Cumulative % Employed for Traditional
Competitive employment	5 (8)	8	1 (4)	4
Individual placement	3 (5)	14	2 (9)	13
Group placement	11 (19)	32	3 (13)	26
Agency-run business	5 (8)	41	2 (9)	35
Sheltered workshop	7 (12)	53	2 (9)	43
Prevocational training	7 (12)	64	3 (13)	57
Unemployed	21 (36)	. . .	10 (43)	. . .
WPS score, mean (SD)	3.64 (2.51)	. . .	3.22 (2.49)	. . .

[a]Values shown as N (%) unless noted otherwise.
Abbreviation: WPS = Work Placement Scale.

DISCUSSION

This naturalistic cross-sectional study provides preliminary information on how atypical antipsychotic agents may affect clinical and work status for clients attending a vocationally oriented psychiatric rehabilitation program. Consistent with the literature, proximal outcomes were significantly associated with the use of atypicals. That is, clients receiving atypicals had significantly fewer symptoms relating to hostility/excitement and to cognitive impairment than did clients receiving traditional antipsychotics. The latter finding is of interest in light of emerging evidence that atypicals may enhance cognitive functioning, both by virtue of their medication action and by the reduced need for and use of anticholinergic medications, which have been associated with cognitive difficulties.[27,71,72]

The difference found in level of hostility/excitement between the defined medication treatment groups also has relevance not only for the ability of individuals with schizophrenia to obtain and maintain employment, but also for other aspects of social functioning. These findings suggest the need for more intensive study of the possible mediating role of cognitive functioning and/or hostility/excitement in the relationship between type of medications prescribed and role functioning.

Our study did not detect significant differences between the treatment groups in EPS or other assessed adverse events. The lack of differences may have reflected the differential use of anticholinergic medication by clients in the traditional group. Another possible explanation concerns the limitation of our checklist approach, which

involved client ratings of discomfort on a list of potential adverse events. More suggestive of the advantages to clients switching to an atypical are study participants' responses to open-ended questions regarding medication use (M.L.M., manuscript in preparation). In the qualitative portion of our interview, clients in the atypical group reported markedly more positive feelings about their medications than did clients in the traditional group. In response to a question about changes experienced by the atypical group after switching medications, some reported feeling less sleepy, feeling less overmedicated, and having an increased ability to concentrate and focus. The open-ended interviews also indicated that a fair proportion of clients treated with atypicals reported weight gain with the switch to an atypical, as others have found.[73]

The finding within the traditional group that those prescribed anticholinergic medications had significantly less severe cognitive symptoms than those who were not was surprising and has not been reported in other studies. In fact, anticholinergic medication use has been associated with memory problems,[72] which, if anything, suggests *greater* cognitive symptoms with its use.

It is also likely that many clients in the atypical group were switched to an atypical agent because of poor response to a traditional antipsychotic; conversely, the clients in the traditional group may have continued taking a traditional antipsychotic by virtue of relatively good response to their medication. Therefore, the clients in the traditional group may have represented a self-selected subgroup of clients with schizophrenia who responded well to this pharmacotherapy regimen, while clients in the atypical group may have had less manageable symptoms.

Linkages Between Clinical and Vocational Status

We found several associations between symptom severity and work status. As have others,[24,29–31,33–35,37,38] we found that poorer cognitive functioning and more severe negative symptoms were negatively related to employment status. However, associations between more severe symptoms on the hostility/excitement factor and work status have not been previously reported.

The study findings could be interpreted to suggest that better control of certain symptoms enabled clients to achieve higher levels of independent employment. Because this is a cross-sectional study, we do not know the direction of causality; studies have found that working in paid employment in integrated settings may improve symptom control.[74,75]

Importantly, 2 of the 3 symptom factors associated with work status were also the factors found to differ between medication treatment groups. Larger past studies have also had difficulties establishing a connection between adverse events and vocational outcomes,[76–78] so the relative lack of connection between these measures and work status in this small study is not surprising.

Employment Status

The employment goal for the psychiatric rehabilitation agency in which the study was conducted was paid employment. Using this standard, the paid employment rate of 50% for study participants compares favorably with the paid employment rate of 27% found in a statewide survey of mental health center clients conducted in Massachusetts.[79] This general level of participation in paid employment within the study sample suggests that the intent of this study—to examine work status among clients receiving professional assistance to achieve this goal—was met.

The fourth hypothesis for the study, that work status would significantly differ between treatment groups, was not supported. On the one hand, these results seem surprising given the findings of other recent studies,[47,49] suggesting that atypical antipsychotic agents may indeed help people with schizophrenia improve their work status. On the other hand, it is important to remember that distal outcomes, such as employment, are influenced by many factors in addition to medications.[44] For example, the level of experienced social support, not assessed in this study, may be another critical component to consider.

The current cross-sectional design was not ideally suited for testing hypothesized pathways of medication effects. Nevertheless, several intriguing findings have emerged from these data, encouraging the investigation of the hypotheses suggested by the findings in larger, prospective samples under more controlled conditions. Our ongoing work includes a prospective longitudinal study to examine the impact of several clinical, cognitive, and treatment variables on work outcomes.

Study Limitations

This study was cross-sectional, evaluating current symptom and work status without evaluating how much improvement or decline that status reflected. It is possible that subjects who had more (or less) severe symptoms or worse (or better) initial work status were more likely to use atypicals.

The insufficient control of treatment histories in this retrospective design posed the largest barrier to clear interpretation of the findings. Length of time taking medication and time in attendance in the psychiatric rehabilitation program were highly variable. Further, the mean time in treatment differed greatly between the groups. Because of the cross-sectional design, it is very difficult to determine the relative influence of these 2 factors. Other treatment factors were also uncontrolled, including the presence of different combinations of psychiatric medications and changes in medications.

The long mean tenure at the psychiatric rehabilitation agency may also limit the generalizability of the study. Clients who continue attending a high-expectation psychiatric rehabilitation program are often individuals who are more likely to succeed in employment than those

who drop out early.[80] Although, overall, neither length of time taking medication nor tenure at the psychiatric rehabilitation program was associated with work status, the study findings may not generalize to clients with a shorter tenure.

The measures used and the methods of data collection represent another set of limitations. We employed a number of measures of convenience, including chart diagnosis, client report of adverse events, and chart review for vocational and medication history. In addition, internal consistency of our clinical scales was modest.

One final, and potentially crucial, limitation is the relatively small sample size. The study may have lacked the statistical power necessary to detect some potential medication effects. Additional longitudinal studies, optimally powered for detecting treatment effects on functional outcomes, are warranted.

CONCLUSION

Increasingly, clients with schizophrenia and related disorders are being prescribed atypical antipsychotics. In this study, clients using atypicals had fewer symptoms of cognitive impairment and fewer symptoms relating to hostility and poor impulse control compared with clients using a traditional antipsychotic. This study also found that less severity of these symptoms was associated with more independent employment status. However, in this cross-sectional study, we did not find a direct association between use of atypicals and achievement of employment in integrated work settings. Nonetheless, more rigorously designed studies with larger sample sizes are warranted to understand the potential role of atypicals in aiding the rehabilitation process for people with schizophrenia.

Drug names: chlorpromazine (Thorazine and others), clozapine (Clozaril and others), haloperidol (Haldol and others), olanzapine (Zyprexa), risperidone (Risperdal), thiothixene (Navane and others), trifluoperazine (Stelazine and others).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

REFERENCES

1. Kinon BJ, Lieberman, JA. Mechanisms of action of atypical antipsychotic drugs: a critical analysis. Psychopharmacology (Berl) 1996;124:2–34
2. McCombs JS, Nichol MB, Stimmel GL, et al. Use patterns for antipsychotic medications in Medicaid patients with schizophrenia. J Clin Psychiatry 1999;60(suppl 19):5–13
3. Wang PS, West JC, Tanielian T, et al. Recent patterns and predictors of antipsychotic medication regimens used to treat schizophrenia and other psychotic disorders. Schizophr Bull 2000;26:451–457
4. Kane JM, Woerner M, Borenstein M. Integrating incidence and prevalence of tardive dyskinesia. Psychopharmacol Bull 1986;22:254–258
5. Marder SR, May PR. Benefits and limitations of neuroleptics—and other forms of treatment—in schizophrenia. Am J Psychother 1986;40:357–369
6. Dixon LB, Lehman AF, Levine J. Conventional antipsychotic medications for schizophrenia. Schizophr Bull 1995;21:567–577
7. Kane JM, Mayerhoff D. Do negative symptoms respond to pharmacological treatment? Br J Psychiatry 1989;155:115–118
8. Dawkins K, Lieberman JA, Lebowitz BD, et al. Antipsychotics: past and future: National Institute of Mental Health Division of Services and Intervention Research workshop, July 14, 1998. Schizophr Bull 1999;25: 395–404
9. Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. Psychiatr Serv 1998;49:196–201
10. Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. Schizophr Bull 1997;23:637–651
11. Olfson M, Mechanic D, Hansell S, et al. Predicting medication noncompliance after hospital discharge among patients with schizophrenia. Psychiatr Serv 2000;51:216–222
12. Ruscher SM, de Wit R, Mazmanian D. Psychiatric patients' attitudes about medication and factors affecting noncompliance. Psychiatr Serv 1997;48: 82–85
13. Expert Consensus Guideline Series: Treatment of Schizophrenia 1999. J Clin Psychiatry 1999;60(suppl 11):1–80
14. Miller AL, Chiles JA, Chiles JK, et al. The Texas Medication Algorithm Project (TMAP) schizophrenia algorithms. J Clin Psychiatry 1999;60: 649–657
15. Casey DE. Side effect profiles of new antipsychotic agents. J Clin Psychiatry 1996;57(suppl 11):40–45
16. Geddes J, Freemantle N, Harrison P, et al. Atypical antipsychotics in the treatment of schizophrenia: systematic overview and meta-regression analysis. BMJ 2000;321:1371–1376
17. Leucht S, Pitschel-Walz G, Abraham D, et al. Efficacy and extrapyramidal side-effects of the new antipsychotics olanzapine, quetiapine, risperidone, and sertindole compared to conventional antipsychotics and placebo: a meta-analysis of randomized controlled trials. Schizophr Res 1999;35: 51–68
18. Tamminga CA. The promise of new drugs for schizophrenia treatment. Can J Psychiatry 1997;42:265–273
19. Grilli Tissot MC, Elkis H. Meta-analyses of randomized controlled trials which compared the effect of typical versus atypical neuroleptics on negative symptoms in schizophrenia [abstract]. Schizophr Res 1999;36:281
20. Moller HJ, Muller H, Borison RL, et al. A path-analytical approach to differentiate between direct and indirect drug effects on negative symptoms in schizophrenic patients: a re-evaluation of the North American risperidone study. Eur Arch Psychiatry Clin Neurosci 1995;245:45–49
21. Tollefson GD, Beasley CM Jr, Tran PV, et al. Olanzapine versus haloperidol in the treatment of schizophrenia and schizoaffective and schizophreniform disorders: results of an international collaborative trial. Am J Psychiatry 1997;154:457–465
22. Tollefson GD, Sanger TM. Negative symptoms: a path analytic approach to a double-blind, placebo- and haloperidol-controlled clinical trial with olanzapine. Am J Psychiatry 1997;154:466–474
23. Keefe RSE, Silva SG, Perkins DO, et al. The effects of atypical antipsychotic drugs on neurocognitive impairment in schizophrenia: a review and meta-analysis. Schizophr Bull 1999;25:201–222
24. Meltzer HY, McGurk SR. The effects of clozapine, risperidone, and olanzapine on cognitive function in schizophrenia. Schizophr Bull 1999;25: 233–255
25. Purdon S, Jones BD, Stip E, et al. Neuropsychological change in early phase schizophrenia during twelve months of treatment with olanzapine, risperidone, or haloperidol. The Canadian Collaborative Group for research in schizophrenia. Arch Gen Psychiatry 2000;57:249–258
26. Lehman AF. Developing an outcomes-oriented approach for the treatment of schizophrenia. J Clin Psychiatry 1999;60(suppl 19):30–37
27. Green MF, Nuechterlein KH. Conceptual frameworks: should schizophrenia be treated as a neurocognitive disorder? Schizophr Bull 1999;25: 309–319
28. Weiden P, Aquila R, Standard J. Atypical antipsychotic drugs and long-term outcome of schizophrenia. J Clin Psychiatry 1996;57(suppl 11): 53–60
29. Bell MD, Lysaker PH. Psychiatric symptoms and work performance among persons with severe mental illness. Psychiatr Serv 1995;46: 508–510
30. Breier A, Schreiber JL, Dyer J, et al. National Institute of Mental Health longitudinal study of chronic schizophrenia: prognosis and predictors of outcome. Arch Gen Psychiatry 1991;48:239–246

31. Davidson L, McGlashan TH. The varied outcomes of schizophrenia. Can J Psychiatry 1997;42:34–43
32. Goldberg RW, Lucksted A, McNary S, et al. Correlates of long-term unemployment among inner-city adults with serious and persistent mental illness. Psychiatr Serv 2001;52:101–103
33. Hoffmann H, Kupper Z. Relationships between social competence, psychopathology and work performance and their predictive value for vocational rehabilitation of schizophrenic outpatients. Schizophr Res 1997; 23:69–79
34. Lysaker P, Bell M. Negative symptoms and vocational impairment in schizophrenia: repeated measurements of work performance over six months. Acta Psychiatr Scand 1995;91:205–208
35. McGurk SR, Meltzer HY. The role of cognition in vocational functioning in schizophrenia. Schizophr Res 2000;45:175–184
36. Collaborative Working Group on Clinical Trial Evaluations. Evaluating the effects of antipsychotics on cognition in schizophrenia. J Clin Psychiatry 1998;59(suppl 12):35–40
37. Green MF. What are the functional consequences of neurocognitive deficits in schizophrenia? Am J Psychiatry 1996;153:321–330
38. Jaeger J, Douglas E. Neuropsychiatric rehabilitation for persistent mental illness. Psychiatr Q 1992;63:71–94
39. Lysaker P, Bell M, Beam-Goulet J. Wisconsin Card Sorting Test and work performance in schizophrenia. Psychiatry Res 1995;56:45–51
40. Franz M, Lis S, Pluddemann K, et al. Conventional versus atypical neuroleptics: subjective quality of life in schizophrenic patients. Br J Psychiatry 1997;170:422–425
41. Meltzer HY, Burnett S, Bastani B, et al. Effects of six months of clozapine treatment on the quality of life of chronic schizophrenic patients. Hosp Community Psychiatry 1990;41:892–897
42. Meltzer HY, Cola P, Way L. Cost effectiveness of clozapine in neuroleptic-resistant schizophrenia. Am J Psychiatry 1993;150:1630–1638
43. Rosenheck R, Tekell J, Peters J, et al. Does participation in psychosocial treatment augment the benefit of clozapine? Arch Gen Psychiatry 1998; 55:618–625
44. Tunis SL, Johnstone BM, Gibson J, et al. Changes in perceived health and functioning as a cost-effectiveness measure for olanzapine versus haloperidol treatment of schizophrenia. J Clin Psychiatry 1999;60(suppl 19): 38–46
45. Lindström LH, Lundberg T. Long-term effect on outcome of clozapine in chronic therapy-resistant schizophrenic patients. Eur Psychiatry 1997;12 (suppl 5):353s–355s
46. Littrell K. Maximizing schizophrenia treatment outcomes: a model for integration. Psychiatr Rehabil J 1995;19:75–77
47. Noordsy DL, O'Keefe C. Effectiveness of combining atypical antipsychotics and psychosocial rehabilitation in a community mental health center setting. J Clin Psychiatry 1999;60(suppl 19):47–53
48. McGurk SR, Bowie CR, Friedman JI, et al. The role of cognitive functioning in vocational outcome in schizophrenia. In: New Research Abstracts of the 153rd Annual Meeting of the American Psychiatric Association; May 16, 2000; Chicago, Ill. Abstract NR374:158
49. Hamilton SH, Edgell ET, Revicki DA, et al. Functional outcomes in schizophrenia: a comparison of olanzapine and haloperidol in a European sample. Int Clin Psychopharmacol 2000;15:245–255
50. Anthony WA, Blanch A. Supported employment for persons who are psychiatrically disabled: an historical and conceptual perspective. Psychosoc Rehabil J 1987;11:5–23
51. Bond GR, Drake RE, Becker DR, et al. Effectiveness of psychiatric rehabilitation approaches for employment of people with severe mental illness. J Disability Policy Studies 1999;10:18–52
52. Bond GR, Drake RE, Mueser KT, et al. An update on supported employment for people with severe mental illness. Psychiatr Serv 1997;48: 335–346
53. Bond GR, Becker DR, Drake RE, et al. Implementing supported employment as an evidence-based practice. Psychiatr Serv 2001;52:313–322
54. Cook J, Razzano L. Vocational rehabilitation for persons with schizophrenia: recent research and implications for practice. Schizophr Bull 2000;26: 87–103
55. Lehman AF. Vocational rehabilitation in schizophrenia. Schizophr Bull 1995;21:645–656
56. Bond GR, Meyer PS. The role of medications in the employment of people with schizophrenia. J Rehabil 1999;65:9–16
57. Corrigan PW, Penn DL. The effects of antipsychotic and antiparkinsonian medication on psychosocial skill learning. Clin Psychol: Science and Practice 1995;2:251–262
58. Schade ML, Corrigan PW, Liberman RP. Prescriptive rehabilitation for severely disabled psychiatric patients. New Dir Ment Health Serv 1990; 45:3–17
59. Schwarzkopf SB, Crilly JF, Silverstein SM. Therapeutic synergism: optimal pharmacotherapy and psychiatric rehabilitation to enhance functional outcome in schizophrenia. Psychiatr Rehabil Skills 1999;3: 124–147
60. Hogarty GE, Goldberg SC. Drug and sociotherapy in the aftercare of schizophrenia patients: one-year relapse rates. Arch Gen Psychiatry 1973;28:54–64
61. Dincin J. A pragmatic approach to psychiatric rehabilitation: lessons from Chicago's Thresholds program. New Dir Ment Health Serv 1995;69: 1–112
62. Cook JA, Razzano L. Discriminant function analysis of competitive employment outcomes in a transitional employment program for persons with severe mental illness. J Voc Rehabil 1995;5:127–139
63. Bond GR, Meyer P, Rollins A, et al. The Impact of Atypical Antipsychotics on Vocational Outcomes in a Psychiatric Rehabilitation Agency: Final Report. Indianapolis, Ind: Indiana University-Purdue University Indianapolis; 1998
64. Meltzer HY. Treatment of the neuroleptic-nonresponsive schizophrenic patient. Schizophr Bull 1992;18:515–542
65. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
66. Kay SR, Fiszbein A, Opler LA. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. Schizophr Bull 1987;13:261–276
67. Bell MD, Lysaker PH, Beam-Goulet JL, et al. Five-component model of schizophrenia: assessing the factorial invariance of the positive and negative syndrome scale. Psychiatry Res 1994;52:295–303
68. Bond GR, Friedmeyer MH. Predictive validity of situational assessment at a psychiatric rehabilitation center. Rehabil Psychol 1987;32:99–112
69. Arns PG, Rogers ES, Cook J, et al. The IAPSRS Toolkit: development, utility, and relation to other performance measurement systems. Psychiatr Rehabil J 2001;25:43–52
70. Lipsey MW. Design Sensitivity. Newbury Park, Calif: Sage; 1990
71. Sup E, Lussier I. Effect of risperidone on cognition in patients with schizophrenia. Can J Psychiatry 1996;41(suppl 8):35–40
72. Spohn HE, Strauss ME. Relation of neuroleptic and anticholinergic medication to cognitive functions in schizophrenia. J Abnorm Psychol 1989; 98:367–380
73. Allison DB, Mentore J, Heo M, et al. Antipsychotic-induced weight gain: a comprehensive research synthesis. Am J Psychiatry 1999;156: 1686–1696
74. Mueser KT, Becker DR, Torrey WC, et al. Work and nonvocational domains of functioning in persons with severe mental illness: a longitudinal analysis. J Nerv Ment Dis 1997;185:419–426
75. Bond GR, Resnick SG, Drake RE, et al. Does competitive employment improve nonvocational outcomes for people with severe mental illness? J Consult Clin Psychol 2001;69:489–501
76. Chacon C, Harper P. Clinical and work performance variables in phenothiazine therapy of schizophrenia. Acta Psychiatr Scand 1973;49:65–76
77. Engelhardt DM, Rudorfer L, Rosen B. Haloperidol and thiothixene in the long-term treatment of chronic schizophrenic outpatients in an urban community: social and vocational adjustment. J Clin Psychiatry 1978;39: 834–840
78. Mintz J, Mintz LI, Hwang SS, et al. Work Outcomes in Depression and Schizophrenia: Final Report. Los Angeles, Calif: UCLA Department of Psychiatry; 1997
79. Rogers ES, Walsh D, Masotta L, et al. Massachusetts Survey of Client Preferences for Community Support Services: Final Report. Boston, Mass: Center for Psychiatric Rehabilitation; 1991
80. Bond GR. Vocational rehabilitation. In: Liberman RP, ed. Handbook of Psychiatric Rehabilitation. New York, NY: Macmillan; 1992:244–275

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