The Effects of Olanzapine and Risperidone on Learning and Retaining Entry-Level Work Skills

Alex Kopelowicz [1], Robert Paul Liberman [1], Charles J. Wallace [1], Fabian Aguirre [2], Jim Mintz [3]

Abstract

Objective: This study compared the effects of olanzapine and risperidone, in combination with work skills training or occupational therapy, on the ability of patients with schizophrenia to learn three different entry-level job tasks. **Methods:** One hundred and twenty stable outpatients with schizophrenia or schizoaffective disorder were randomly assigned to open-label risperidone or olanzapine. After four weeks of treatment, subjects were randomly assigned to receive either work skills training or occupational therapy. Work skills training consisted of six sixty-minute sessions designed to train subjects on three entry-level job tasks. Occupational therapy sessions were matched for time and therapist attention. Subjects were assessed on psychiatric symptoms, level of functioning, side effects, and acquisition and retention of work skills at baseline, after four weeks on study medication, and at twelve and twenty-four weeks after study entry. **Results:** Subjects assigned to work skills training learned all three work tasks and retained two of the tasks significantly better than subjects assigned to occupational therapy. There were minimal differences between subjects assigned to risperidone and olanzapine. **Conclusions:** Patients with schizophrenia and schizoaffective disorder were able to learn and retain entry-level job skills while taking either antipsychotic medication. The highly structured skills-training protocol used to teach entry-level job skills was prepotent over the pharmacological effects of antipsychotic medication. Future research is needed on the interaction between medications and skills training on key psychosocial outcomes such as the work functioning of patients with schizophrenia.

Key Words: Schizophrenia, Antipsychotic Medications, Risperidone, Olanzapine, Work Skills, Skills Training, Vocational Rehabilitation

[1] *Department of Psychiatry and Biobehavioral Sciences, Geffen School of Medicine at UCLA*
[2] *Department of Psychology, University of Texas, Austin*
[3] *Department of Psychiatry, University of Texas Health Sciences Center at San Antonio*

Address for correspondence: Alex Kopelowicz, MD, San Fernando Mental Health Center, 10605 Balboa Blvd., Suite 100, Granada Hills, CA 91344
Phone: (818) 832-2400; Fax: (818) 832-2567;
E-mail: akopel@ucla.edu

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Introduction

Controlled efficacy trials of both first- and second-generation antipsychotic medications have defined outcome almost exclusively in terms of reduction in symptoms and prevention of hospitalization (1, 2). However, with the current focus on patients' recovery and movement to assuming valued societal roles (e.g., student, wage earner, spouse), the definition of outcome has expanded from symptom reduction to improvement in social functioning. A corresponding hope has been that second-generation antipsychotic medications may improve social and work functioning through greater control of negative symptoms and depression, decreased levels of extrapyramidal side effects, and improved cognitive functioning (3). The few studies that have investigated the effects of second-generation antipsychotic medi-

Clinical Implications

This study demonstrated minimal differences between risperidone and olanzapine on the performance of entry-level job skills by individuals with schizophrenia. Thus, there was no evidence of a direct effect of either second-generation antipsychotic on work functioning, which is consistent with most of the previous literature (6-12). However, the study did support the value of behaviorally oriented instruction to improve work skill performance in individuals with schizophrenia. Moreover, by demonstrating change over time with training, the study highlighted the utility of performance-based measures of functional capacity (i.e., the work tasks used in this project) as a less environmentally dependent (e.g., local economic conditions, disincentives to work) alternative to actual employment outcomes as a means to focus on work capacity (32).

cations on community and role functioning have reported mixed results. Hamilton et al. (4) found that, compared to haloperidol, patients randomized to receive olanzapine reported a 20% or greater improvement in the quality of their lives, spent 75% or more of their time in useful work, and socialized more than once a month over the course of one year. Aquila and Weiden (5) retrospectively evaluated the vocational status of a cohort of hospitalized patients with schizophrenia. They noted that vocational outcomes were better for patients receiving olanzapine compared to those receiving conventional antipsychotic medications, a finding similar to that reported by Rosenheck and colleagues (6) in a randomized, controlled comparison of clozapine and haloperidol.

In contrast, several recent studies (7-11) and one review of the literature (12) found few differences in employment outcomes between first- and second-generation antipsychotics. Comparisons of second-generation antipsychotics are even rarer; only one naturalistic study has compared two second-generation agents (risperidone and olanzapine) on work outcome and reported no difference between them (9).

The variable and inconclusive results on vocational functioning from studies comparing first- and second-generation antipsychotics may stem from flaws in the studies' designs, such as small sample sizes, lack of randomization, failure to measure levels of participation in work and the presence of disincentives to work. To overcome these obstacles, we chose a research design in which participants would be evaluated on work domains developed and validated by our research group over the past ten years that represent typical entry-level job opportunities for people with serious mental disorders. To date, no prospective, randomized controlled research has examined the interactions between second-generation antipsychotic medications and vocational interventions on work performance. In a randomized clinical trial, we compared the effects of olanzapine versus risperidone on the performance of entry-level job skills by individuals with schizophrenia participating in two-week regimens of either 1) work skills training or 2) cognitively enhancing, expressive occupational therapy.

Methods

Subjects

Subjects were one hundred and twenty English-speaking outpatients receiving treatment at a community mental health center in the northern section of Los Angeles County. Subjects were recruited by first asking clinicians at the mental health center to refer outpatients who would be interested in participating in a study designed to evaluate the effect of medication on learning entry-level work skills. All subjects were diagnosed with either schizophrenia or schizoaffective disorder, and diagnoses were confirmed by the results of the Structured Clinical Interview for DSM-IV (SCID; 13) conducted by an interviewer trained to reliability at the UCLA Clinical Research Center for Schizophrenia. All subjects were between 18 and 64 years of age and had been living in Los Angeles County for at least six months. None met the criteria for the deficit syndrome (14); had abused or been dependent on alcohol or illegal substances within the previous three months; had received psychiatric inpatient treatment within the previous six months; had a history of neurological disorder apart from schizophrenia; or, had a change in antipsychotic medications (type and dosage) in the previous three months. These criteria were designed to select subjects who were clinically stable, had dependable residential arrangements, and required maintenance antipsychotic medications. These characteristics approximated those of patients eligible for referral to work programs at most mental health centers, but may not represent the overall population of patients who may include less interested or motivated participants.

After describing the study to prospective subjects, informed consent was obtained in accordance with procedures set forth by the Internal Review Board of the University of California, Los Angeles. Once informed consent was obtained, an appointment was scheduled to administer the SCID. If the results of the SCID confirmed the diagnosis and all other inclusion/exclusion criteria were fulfilled, an appointment was scheduled to administer the pre-test for all of the study's measures. Subjects received $10.00 per hour for their participation, including all assessments. The maxi-

mum amount a subject could receive for participating in the study was $160.00 (six hours of training and ten hours of assessment over the six-month protocol).

Procedure

After the pre-tests were administered, subjects were tapered off their previous antipsychotic medication (see Table 1 for baseline medications) for a two-day period and were then randomly assigned to receive either olanzapine or risperidone using a computerized table of numbers randomly allocated to one of the two medications, with titration determined by the subjects' treating psychiatrists. Both the subjects and their psychiatrists were informed about the medication to which subjects had been assigned, and the psychiatrists prescribed medications within a range of 5 to 20 mg/day for olanzapine and 2 to 8 mg/day for risperidone. The psychiatrists based the dosage on their judgments of the optimum balance of maximum symptom control and minimal side effects. The mean modal dose for subjects assigned to olanzapine was 15.7±3.4 (standard deviation=SD) mg and to risperidone was 3.7±1.8 (SD) mg.

After four weeks of treatment with either risperidone or olanzapine, subjects were randomly assigned to receive either work skills training (WT) or expressive occupational therapy (OT) using a block allocation of six to eight participants per group to facilitate subject flow. The WT and OT groups were conducted by the same certified occupational therapists to minimize the potential effect of bias (e.g., better occupational therapists assigned to one intervention but not the other). Both interventions were delivered in English and conducted with groups of six to eight subjects for six sixty-minute sessions administered during a two-week period. The schedule and duration of the OT sessions were yoked to those of the WT group. To ensure fidelity of the work skills training, the occupational therapists were trained to conduct the WT procedures by project personnel to a criterion of 95% correct. Project personnel continued to periodically observe the accuracy of the WT sessions throughout the protocol. No fidelity measurements were conducted for the OT group.

Work Skills Training

Three entry-level work tasks were trained in the six sessions of the WT condition: 1) one session on filing index cards in alphabetical order; 2) one session on selecting and inserting parts into a computer motherboard; and, 3) four sessions on using WordPad, the simple word processor that is part of the Microsoft Windows® operating system. The specific details of the six WT sessions are described fully in another article (15). To briefly summarize, the trainers utilized basic principles of learning, including the provision of specific instructions, demonstration of the skill to be learned, prompting and coaching, shaping, corrective feedback and contingent positive reinforcement.

Index Card Filing: This work task trained subjects to file materials in a prescribed order. Subjects were given piles of twenty index cards, each of which contained information about the purchaser of an automobile. The information was printed in 20-point, Arial font and listed the city in which the automobile had been purchased, the name of the manufacturer, and the last name of the purchaser. Subjects were asked to file each card into the box that was labeled on the outside with the name of the city, then into the section in the box that was labeled with the name of the car manufacturer, then into the section (A-G, H-L, M-R, S-Z) with the first letter of the purchaser's name, and finally in alphabetical order within this section. Once subjects completed a twenty-card pile, a new pile was placed before them, up to a maximum of eighty cards.

Training was conducted for a practice pile of twenty-five cards. The trainers first instructed subjects in the correct sorting method, demonstrated it, and then asked subjects to practice. After subjects placed the first practice card, the trainers provided feedback about the sorting of that card, noting what had been correctly sorted and what had not been. They demonstrated the correct sorting procedure, and asked subjects to redo their sorting. Trainers provided feedback about the repeat sorting and continued with the next practice card until all twenty-five had been presented. Then they placed the first pile of twenty cards in front of the subjects.

Computer Assembly: This assembly line work task trained subjects to select and insert parts into a computer motherboard in a prescribed sequence. Subjects were seated in front of a workbench on which a computer motherboard had been placed, surrounded by various computer parts, some of which were to be inserted into the motherboard and others that were distracters. During a thirty-five minute training session, the trainer stood in front of a poster that listed the order in which the parts were to be inserted, held each part high enough so subjects could see it, named the part (e.g., "DDR memory chip"), and then demonstrated the exact method of inserting it. The trainer then asked subjects to practice inserting each part and walked around the room, correcting the subjects' mistakes.

At the end of the training, the poster was removed, and subjects were told to begin. Subjects worked for fifteen minutes on the assembly task. As they completed one motherboard, the trainer removed it, and another bare motherboard and parts were placed on the workbench.

Word Processing: This activity trained participants how to use the simple word processor that is supplied with the

Microsoft Windows® operating system, WordPad. Training was conducted in four sessions designed to teach subjects how to: 1) identify and manipulate the computer's hardware; 2) select, delete, replace, add, copy, move and store text; 3) format text and paragraphs; and, 4) print a document. The four sessions consisted of two one-hour morning sessions and two one-hour afternoon sessions. During the morning sessions, the trainer read aloud the text printed in the "Trainer's Manual" and displayed graphics, primarily screen shots, on an overhead projector. The graphics were also printed in a "Participant's Workbook," and subjects could follow the workbook as the trainer read the text and displayed the same graphics on the overhead projector. The trainer also answered subjects' questions, consistent with the need to present and illustrate all the material in each section. The trainer asked subjects to perform many of the actions that were demonstrated in the screen shots and then walked around the room, helping any who were having difficulty performing the actions. The afternoon sessions were structured as additional practice of the actions specified in the morning sessions.

After completing the six sessions of WT, subjects were not provided with formal opportunities to practice these skills, although there was no attempt to control or measure the subjects' subsequent exposure to the tasks; for example, accessing a computer to try out newly learned word processing skills. Most employers, of course, would put newly trained employees immediately into the work setting to join other trained employees. However, the goal in this study was to measure retention over the subsequent twelve weeks.

Occupational Therapy

As a control condition to contrast with WT, the occupational therapists conducted six OT sessions following a format utilized in previous projects (16). OT included participation in expressive, creative, and artistic activities with therapeutic feedback, encouragement and practice intended to increase attention, independence of effort, sustained performance, self-esteem, assertiveness, socialization, and group participation (17).

Measures

Work Skills Training Assessments

Index Card Filing: One point was given for correctly sorting each card by city, car make, alphabet section, and alphabet order, for a total of up to four points for each card. Subjects sorted for 15 minutes to a maximum of 80 cards, and the total points earned in the 15 minutes was the dependent variable.

Computer Assembly: One point was given for correctly inserting each part that required only force for insertion (e.g., AGP graphics card) and two points for correctly inserting parts that required both force and latching (e.g., DDR memory). In addition, one point was awarded for assembling the parts in the order listed on the poster board. The dependent measure was the total number of points earned in the 15 minutes of assembly.

Word Processing: Subjects were given 30 minutes to answer a 52-item, multiple-choice and true/false test that covered the specific material given in the four training sessions. The dependent measure was the total number of questions answered correctly.

Psychometric Characteristics of the WT Dependent Measures: The index card filing task has demonstrated good social and construct validity, and the scoring method has been shown to be reliable (18, 19). In addition, the internal consistencies of all three WT dependent measures were calculated using data for all 120 subjects at their enrollment in the study, before assignment to risperidone or olanzapine. For the 4 piles of cards of the filing task, coefficient alpha was 0.84; for the 7 parts inserted into the motherboard, it was 0.92; and, for the 52 items of the test of computer knowledge, it was 0.91. The test-retest reliabilities of the 3 WT dependent measures were calculated using the data for the 60 OT subjects at the 4-week and 12-week testings. None of the OT subjects, of course, participated in the WT training. The test-retest correlation over the 8-week interval for the filing task was 0.78; for the assembly task, 0.82; and, for the knowledge task, 0.94. No attempt was made to provide validation of the three tasks as measures of "generic" skills. Rather, they were specifically designed as tasks to be trained, and their retention determined over a succeeding interval.

Clinical Dependent Measures

Expanded Brief Psychiatric Rating Scale: The 24-item UCLA Expanded BPRS (20) is a semi-structured interview that combines a respondent's self report with the interviewer's observations to obtain seven-point ratings of a respondent's psychopathology (e.g., delusions, suicidality). Project interviewers were trained to reliability (kappa=.87) by the Diagnostic and Psychopathology Unit of the UCLA Research Center for Treatment and Rehabilitation of Psychosis. Raters were blind to the subjects' training group and medication group assignments.

Clinical Global Impression Scale (CGI; 21): Scores for the single item of the CGI range from 1 to 7, with higher scores indicating greater severity of illness.

Calgary Depression Scale (CDS; 22): The CDS is a nine-item self-report instrument specifically designed for assessing depression in schizophrenia by minimizing overlap with extrapyramidal or negative symptoms.

Extrapyramidal Syndrome Rating Scale (ESRS; 23): The incidence and degree of neurological side effects were assessed with the twelve-item ESRS.

Administration of Dependent Measures

All measures were administered to the subjects at enrollment in the study, and 4, 12, and 24 weeks later (referred to as baseline, Week 4, Week 12 and Week 24, respectively). Additionally, for the WT subjects, the work skills measures were administered at the six-week point (referred to as Week 6) to determine the immediate effect of the training.

Data Analysis

The design of the study was a 2x2 factorial with repeated measures: two between-subjects factors, training group (WT and OT) and medication (olanzapine and risperidone), and one within-subjects factor, time of testing. The data analyses were designed to answer four questions. First, did the subjects improve their performance on the tasks during the four-week titration of study medication, prior to receiving work skills training? To answer this question, an ANOVA was conducted separately for each task with one between-subjects factor, medication, and one within-subjects factor, testing time (baseline versus Week 4).

Second, did the WT subjects learn the tasks during the two weeks of WT sessions? To answer this question, an ANCOVA was conducted separately for each task with one between-subjects factor, medication, and one within-subjects factor, testing time (pre-training/Week 4 versus post-training/Week 6). The covariate in each analysis was the baseline job skill score.

Third, did the medications affect the subjects' retention of the tasks? To answer this question, an intent-to-treat analysis was conducted separately for each of the job skill measures using all subjects randomized to a condition regardless of degree of participation as long as there were two assessment points (at enrollment and at least one other time point). The data were analyzed with a mixed-model factorial ANCOVA with repeated measures using SAS/Mixed (24) with two between-subjects factors, training group and medication, and one within-subjects factor, time of testing (Weeks 12 and 24). Score at Week 4 was included as a covariate.

Fourth, were there any differences between medications in subjects' clinical functioning throughout the study period and, if so, were there significant correlations between any of these measures and performance on the work task? To answer this question, an intent-to-treat analysis was conducted separately for each clinical measure using a mixed-model factorial ANCOVA with one between-subjects factor, medication, and one within-subjects variable, time of testing (Weeks 4, 12, and 24), with baseline as a covariate. Correlations were calculated between 1) changes in symptom; 2) functioning; and, 3) extrapyramidal side effect ratings and changes in work task scores.

Results

Demographic and Clinical Characteristics

The demographic and clinical characteristics of the subjects at enrollment are presented in Table 1. All of the subjects were taking only one antipsychotic medication at baseline. No significant differences were found between the olanzapine and risperidone groups at baseline for illness, treatment, or demographic characteristics. There was no significant difference in dropouts between the two medication groups; 80% of subjects assigned to olanzapine and 78% assigned to risperidone completed all of the assessments throughout the protocol.

Did the subjects learn the tasks during the medication titration (pre-training) period? Six subjects (olanzapine=2; risperidone=4) who were randomized to a medication group dropped out before the first post-baseline evaluation (Week

Table 1 Demographic and Clinical Characteristics of Subjects on Olanzapine versus Risperidone

	Olanzapine (n=60)	Risperidone (n=60)
Age in years, mean (SD)	37.0 (11.9)	36.6 (11.1)
Illness chronicity in years, mean (SD)	13.5 (6.4)	14.2 (7.0)
Education in years, mean (SD)	11.9 (2.1)	12.5 (2.4)
Gender, no. males (%)	43 (71)	39 (65)
Ethnicity, no. (%)		
African American	4 (7)	7 (12)
Asian	1 (2)	3 (5)
Hispanic	32 (53)	23 (38)
Caucasian	23 (38)	27 (45)
Marital status, no. unmarried (%)	55 (92)	53 (88)
Employment, no. unemployed (%)	55 (92)	45 (75)
Cigarette smokers, no. (%)	33 (57)	39 (65)
Baseline antipsychotics, no. (%)		
Conventional	30 (50)	28 (47)
Quetiapine	12 (20)	10 (17)
Ziprasidone	6 (10)	7 (12)
Aripiprazole	4 (7)	6 (10)
Risperidone	5 (8)	4 (7)
Olanzapine	3 (5)	5 (8)
BPRS*, mean (SD)	61.9 (25.4)	57.5 (25.4)
CGI-S†, mean (SD)	4.4 (0.74)	4.3 (0.51)
CDS‡, mean (SD)	9.0 (7.9)	8.3 (7.2)

*Brief Psychiatric Rating Scale: 24 items rated "1" (symptom is not observed) to "7" (symptom is very severe); †Clinical Global Impression-Severity scale: rated "1" (not at all ill) to "7" (extremely severe); ‡Calgary Depression Scale: 9 items rated "0" (absent) to "3" (severe).

Table 2 Scores on Work Tasks at Baseline, before Work Skills Training (Week 4) and Immediately after Training (Week 6), for Subjects in each of the Two Drug Groups, Olanzapine (OLZ) and Risperidone (RIS)

		Raw Means			Analysis[§]								
					Time Main Effects			Drug Main Effects			Drug-by-Time Interaction		
		Baseline* n=60 Mean (SD)	Week 4[†] n=56 Mean (SD)	Week 6[‡] n=56 Mean (SD)	F	df	p	F	df	p	F	df	p
Computer Assembly Task (max score=36)	RIS	3.0 (5.4)	4.2 (6.6)	26.3 (4.5)	613.5	1,53	.0001	.34	1,53	NS	.63	1,53	NS
	OLZ	7.6 (8.8)	8.5 (9.7)	27.5 (3.7)									
Word Processing Task (max score=52)	RIS	29.5 (9.9)	29.3 (9.1)	34.0 (8.8)	3.6	1,53	.06	.15	1,53	NS	.87	1,53	NS
	OLZ	27.2 (9.0)	28.2 (9.7)	32.9 (8.8)									
Index Card Filing Task (max score=360)	RIS	138.4 (56.0)	151.0 (60.7)	182.4 (70.5)	12.6	1,53	.001	.67	1,53	NS	.42	1,53	NS
	OLZ	141.7 (68.5)	153.9 (66.8)	192.4 (68.2)									

*Baseline: before randomization to medication condition (olanzapine vs. risperidone); [†]Week 4: before commencement of training groups; [‡]Week 6: post-test conducted immediately after two weeks of training; [§]Based on an ANCOVA using baseline as a covariate, comparing Week 4 to Week 6, with drug condition and time as independent variables; NS=not significant.

4). For all three tasks, there were no significant main effects for medication or time or any interaction effects (all p>.30). Subjects' scores at baseline and Week 4 were virtually identical (see Table 2). These results suggest that prior to work skills training, neither medication alone nor time (i.e., practice effects) led to improved task performance.

Did WT subjects learn the tasks during the training period? Four of the subjects who had been randomized to the WT group dropped out of the research before training began. For all three tasks, the main effect of time was significant, albeit marginally so, for word processing (computer assembly: F=613.5, p<.0001; word processing: F=3.6, p=.06; all three df=1,53; index card filing: F=12.6, p<.001). These results suggest that the work training was effective (see Table 2). There was no main effect of medication nor medication x time interaction effects for all three tasks. Thus, there was no evidence that the medications differentially affected learning.

Did the medications affect retention of the task skills? The results for retention of the three job tasks at Weeks 12 and 24 are presented in Table 3 and Figure 1. For the computer assembly measure, there was a significant main effect for training (F=69.8, df=1,99, p<.001) and a significant training by time interaction (F=4.0, df=2,99, p<.05), indicating that WT resulted in higher scores than OT across time and that WT subjects performed better than OT subjects regardless of medication type. In addition, there was a trend level effect for time (F=3.5, df=1,99, p=.07), indicating that all groups on average may have improved over time, perhaps as the result of a practice effect (after four assessment periods). Main and interaction effects involving medication type were statistically nonsignificant.

For the word processing measure, there was a significant main effect for training (F=4.5, df=1,99, p<.04) but not for time or medication. As with computer assembly, the main effect of training reflects the benefits of the WT intervention. There were no significant two-way interactions, but there was a significant three-way interaction (F=5.9, df=2,99, p=.02). This interaction reflects a differential effect of the three factors (medication x training type x time). For both medications, the WT intervention resulted in the expected increase from the Week 4 to the Week 12 time points, but there was a subsequent performance decline for the olanzapine group compared to an additional performance increase in the risperidone group to the point that the medication groups were significantly different at the Week 24 testing (t=2.32, p=.02) (see Figure 1).

For the index card filing measure, there were no significant main effects or interactions. Despite the increase in performance from Weeks 4 to 6 for the WT group, the effect of training did not persist beyond Week 6. Both groups' performance across the 12- and 24-week time points was not appreciably different.

Did the medications' impact on clinical measures affect task performance? Both medication groups improved significantly relative to baseline scores on the BPRS (F=22.68, df=3,116, p<.0001), the CDS (F=38.3, df=3,116, p<.0001), and on the CGI (F=49.8, df=3,116, p<.0001). There were no medication differences on these measures. Subjects on olanzapine experienced significantly less extrapyramidal

Table 3 Change in Scores on Three Work Tasks from before Psychosocial Treatment (Week 4) to Six Weeks (Week 12) and Eighteen Weeks after Training (Week 24) for Subjects in each of the Two Training Conditions, Work Training (WT) and Occupational Therapy (OT), and each of Two Drug Groups, Olanzapine (OLZ) and Risperidone (RIS)

Work Tasks		Least Square Means Adjusted for Scores at Week 4*		Analysis†											
		Week 12 n=106 Mean (SD)	Week 24 n=96 Mean (SD)	Time Main Effects			Training Group Main Effects			Drug Main Effects			Training Group by Drug-by-Time Interaction		
				F	df	p	F	df	p	F	df	p	F	df	p
Computer Assembly Task (max score=36)	RIS/WT	11.3 (1.3)	13.5 (1.4)	3.5	1,99	.07	69.8	1,99	.001	2.5	1,99	NS	.58	2,99	NS
	RIS/OT	2.1 (1.2)	1.3 (1.3)												
	OLZ/WT	9.0 (1.2)	11.0 (1.3)												
	OLZ/OT	-.04 (1.4)	0.6 (1.5)												
Word Processing Task (max score=52)	RIS/WT	2.5 (1.0)	4.3 (1.2)	.15	1,99	NS	4.5	1,99	.04	1.8	1,99	NS	5.9	2,99	.02
	RIS/OT	1.0 (1.0)	-0.3 (1.1)												
	OLZ/WT	1.8 (1.0)	0.4 (1.1)												
	OLZ/OT	0.2 (1.1)	0.0 (1.3)												
Index Card Filing Task (max score=360)	RIS/WT	11.6 (8.4)	-1.5 (11.2)	.17	1,99	NS	1.0	1,99	NS	0.1	1,99	NS	1.5	2,99	NS
	RIS/OT	10.2 (7.6)	11.1 (10.2)												
	OLZ/WT	-3.6 (7.6)	3.6 (9.9)												
	OLZ/OT	12.8 (8.9)	9.7 (11.4)												

*Higher scores indicate improved task performance; †Based on a 2x2 factorial, mixed-model repeated measures ANCOVA (SAS mixed), using Week 4 score as a covariate, with training, drug condition, and follow-up time as independent variables; NS=not significant.

side effects than subjects on risperidone (F=12.5, df=3,116, p<.001). Six patients (10%) on risperidone and four patients (7%) on olanzapine received anticholinergic medication for extrapyramidal side effects during the study period. There were no significant correlations between clinical symptoms, psychosocial functioning, extrapyramidal side effects or use of anticholinergic medications with performance on any of the job task skills (all p-values >.30).

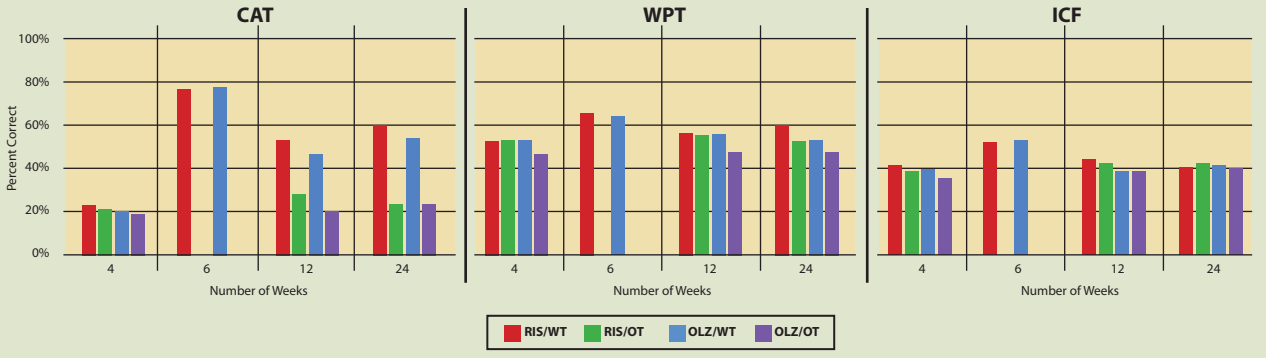
Discussion

The present study compared the effects of olanzapine and risperidone, in combination with work skills training or occupational therapy, on the ability of clinically stable outpatients with schizophrenia to learn and retain three different entry-level job tasks. Although not the main focus of this research, the clearest finding of this study was that subjects assigned to work skills training were able to learn three entry-level job tasks regardless of which medication they were taking. The efficacy of skills training has been shown in numerous studies (see reference 25 for a review), but more specifically, the results of this study are consistent with previous work from our group (19) that demonstrated the utility of skills-training techniques for teaching entry-level work skills. As in that study, the highly structured, skills-training protocol used to teach entry-level job skills was prepotent over the pharmacological effects of antipsychotic medication. There was no significant difference in learning between subjects assigned to either medication on any of the job tasks. However, on one of these job tasks (i.e., word processing), subjects assigned to risperidone demonstrated modestly better skill retention at the 24-week assessment point than those subjects assigned to olanzapine.

Although it has been suggested that second-generation antipsychotic medications may improve patients' social/work functioning by reducing negative symptoms, decreasing motor side effects, and improving depression (26), we found no evidence that skill learning was correlated with improvements in symptoms, side effects, or psychosocial functioning. The possibility remains that the putative effect of second-generation medications on improving cognitive functioning (27-29) may help patients benefit from the therapies that teach them the skills they lack; however, this study did not test that hypothesis.

There were several other limitations of this study. First, two of the job tasks (word processing test and computer assembly task) have not been psychometrically validated. Second, although assessors were blinded, clinicians were not. In some ways, that could be viewed as a strength because it indicates that the study was more of an effectiveness trial with results that are consequently more generalizable. In addition, the feasibility of conducting this study in a typical community mental health center would have been reduced if psychiatrists were blinded to medication condition. Third, it is not certain that improvements on the work tasks

Figure 1 **Performance on Computer Assembly Task (CAT), Word Processing Test (WPT), and Index Card Filing (ICF) for Subjects in each of the Two Training Conditions, Work Training (WT) or Occupational Therapy (OT), and each of the Two Medications, Olanzapine (OLZ) and Risperidone (RIS), across Time***



*Estimated scores derived from a 2X2 factorial, mixed-model repeated measures ANCOVA (SAS mixed), with training, drug conditions, and follow-up time as independent variables. Values are adjusted for baseline values and linear effects of time within each group.

would generalize to the real world, competitive job environment. In fact, the work tasks were designed specifically to insure that other, nonexperimental influences and variables would not interfere with the need to evaluate sensitive effects and interactions. Nevertheless, this limitation is mitigated somewhat by the fact that each of the work tasks are represented in entry-level jobs in the community, and one of the tasks (i.e., index card filing) was socially validated with employers and vocational rehabilitation counselors (18). Fourth, we did not measure potential adverse effects other than extrapyramidal symptoms (e.g., weight gain, metabolic parameters, prolactin levels) as we did not expect these variables to have a direct influence on the ability to learn the work tasks. Fifth, the study population only included patients who were deemed by their clinicians to be interested in returning to work, thus the results cannot be generalized to the larger group of patients diagnosed with schizophrenia or schizoaffective disorder. Finally, we only studied two of the second-generation antipsychotic agents and thus cannot comment on the potential benefits of other medications in this class. However, large-scale studies comparing several antipsychotic medications (including the ones examined in this study) have found minimal differences on psychosocial functioning (11, 30, 31).

Conclusions

In summary, this study demonstrated minimal differences between risperidone and olanzapine on the performance of entry-level job skills by individuals with schizophrenia. Thus, there was no evidence of a direct effect of either second-generation antipsychotic on work functioning, which is consistent with most of the previous literature (6-12). However, the study did support the value of behaviorally oriented instruction to improve work skill performance in individuals with schizophrenia. Moreover, by demonstrating change over time with training, the study highlighted the utility of performance-based measures of functional capacity (i.e., the work tasks used in this project) as a less environmentally dependent (e.g., local economic conditions, disincentives to work) alternative to actual employment outcomes as a means to focus on work capacity (32).

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