# Assessing the Utility of Atypical Antipsychotic Medication in Adults With Mild Mental Retardation and Comorbid Psychiatric Disorders

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***Objective:*** Research on psychiatric outcomes among individuals dually diagnosed with mild mental retardation and co-occurring mental illness who are treated with antipsychotic medication is markedly limited due to difficulties encountered in (1) making valid and reliable psychiatric diagnoses and (2) accurately rating and following psychiatric symptom change over time in this specialty population.

***Method:*** To address these issues, DSM-IV psychiatric diagnoses were made by an experienced dual-diagnosis clinician, and the Aberrant Behavior Checklist (ABC) and the Global Assessment of Functioning were used to assess behavioral and psychiatric features in a psychiatric partial hospital setting. Data were collected by chart review from 72 patients admitted consecutively from January 1998 to December 1999. Assessments were compared at admission and discharge in this retrospective study for 3 treatment groups that were defined by antipsychotic medication status at discharge: no antipsychotic (N = 15), atypical antipsychotic only (N = 41), and mixed atypical/typical antipsychotics or typical antipsychotic only (N = 16).

***Results:*** Improvement on the ABC social withdrawal subscale was greater for atypical antipsychotic medication–treated, dually diagnosed patients than for those who received other treatment regimens. In addition, a dose-response relationship was observed for this subscale and atypical antipsychotic medication dose.

***Conclusion:*** For certain psychotic patients with mild mental retardation, the atypical antipsychotics may be an appropriate and effective treatment modality.

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Psychotic symptoms are widely recognized among individuals with mental retardation and developmental disability, however difficult it might be to discriminate these symptoms from baseline features of mental retardation itself.[1,2] The prevalence of recognized psychotic illness among adults with mental retardation is in the range of 3% to 6%.[3] This includes the 3% to 3.5% with comorbid schizophrenia and some portion of the 1.2% to 1.9% who are diagnosed with mood disorders including psychotic depression and bipolar disorder with psychosis.[3] Although experts in the field have made important contributions in recent years,[4–6] efficacious psychopharmacology in the treatment of adults with mental retardation and coexisting psychiatric features, the so-called "dually diagnosed," remains elusive.[7]

While several investigators have reported on the use of the atypical antipsychotics (newer, or novel, antipsychotic agents) in adults with mental retardation and developmental disability, the focus of treatment in these reports has usually been the treatment of severely disturbed, aggressive, and self-abusive behaviors.[8–13] However, one of the cited studies[13] was later criticized[14] for a primary failure to diagnose and treat the underlying psychiatric etiology of the behavioral disturbances reported among the mental retardation/developmental disability patients included in their report. In Aman and Madrid's review of the use of atypical antipsychotics in the mental retardation/developmental disability population,[15] 3 major categories of the use of these medications are specified: (1) mental

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retardation and comorbid psychiatric syndromes, (2) mental retardation and behavioral problems, and (3) autism and pervasive developmental disorders. These authors conclude that the atypical antipsychotics are efficacious both in the treatment of psychotic symptoms and in reducing behavioral symptoms in individuals with mental retardation.

The literature does include several published studies on the use of the atypical antipsychotics in patients with mental retardation/developmental disability and identified, comorbid psychiatric symptoms; however, the individuals reviewed in these reports were largely those with advanced levels of intellectual disability. These studies include 1 by Antonacci,[16] who reviewed 8 published reports including 142 patients of the use of risperidone in a range of individuals with dual diagnosis and moderate to severe and profound mental retardation. Simon et al.[17] reported improvement in 10 patients with moderate to severe mental retardation and co-occurring psychiatric diagnoses with the substitution of risperidone for typical antipsychotics. Vanden Borre et al.[18] reported improvement in 37 patients with persistent behavioral disturbances with the add-on use of risperidone in one of the few double-blind, crossover protocols utilizing an atypical antipsychotic in patients with mental retardation/developmental disability.

Friedlander et al.[19] reported a chart review study in which 42 adolescents with mental retardation/developmental disability ranging from borderline to severe who had been prescribed atypical antipsychotic medications were identified. Patients with diagnoses of behavioral and neurologic disorders were included in the sample, but a majority of the subjects were diagnosed with psychotic disorders. These authors report significant clinical improvement associated with the use of atypical antipsychotics in 57% of the subjects who were taking risperidone or olanzapine.

Overall, studies restricted to patients with mental retardation/developmental disability who are prescribed typical (older) or atypical (newer) antipsychotics for the treatment of diagnosed psychotic disorders, rather than for behavioral disturbances, are underrepresented in the literature except for the use of clozapine. Sajatovic et al.[20] and Antonacci and de Groot,[21] reporting on psychotic patients with mild mental retardation, and Buzan et al.,[22] reporting on patients with moderate to profound mental retardation, all report improvement in these populations during the use of clozapine. Regulatory issues involved in the use of clozapine are likely to be responsible for this difference from the other antipsychotics in mental retardation/developmental disability, as the use of clozapine was restricted by pharmaceutical companies to those with psychotic symptoms.

A fundamental issue for interpretation of response-to-treatment studies among those with mental retardation relates to the choice of clinical instruments used to identify psychotic thinking and to assess change over time. Psychotic symptoms presenting in those with dual diagnosis can be either over- or underdiagnosed due to the limitations of an interviewer's ability to appreciate the internal experience of an individual with mental retardation. This over- or underdiagnosis is due, in part, to cognitive and communication deficits found commonly in those with even mild mental retardation or borderline IQ. Most psychiatric rating scales employed in patients with psychotic symptoms, such as the Brief Psychiatric Rating Scale,[23] rely in part on the affected individual's ability to introspect internal states, such as mood and perception, and to reliably report these symptoms to an interviewer. In addition, the use of these rating scales to assess change over time requires a patient to report an increase or a decrease in these internal states and perceptions, a process that many with mental retardation/developmental disability are unable to conceptualize or to accurately perform. Valid outcomes research with these dually diagnosed patients requires the employment of assessment tools that function acceptably well even when these introspective skills are compromised or largely absent. We believe that one of the few assessment instruments that satisfies this requirement is the Aberrant Behavior Checklist (ABC).[24] The ABC, a structured instrument developed for use in patients with moderate to severe and profound mental retardation, relies exclusively on reliably observable phenomena in order to avoid misinterpretation of internal states, such as the experience of psychosis.

The current study examined treatment outcome in patients with mild mental retardation and comorbid DSM-IV, Axis I,[25] clinical, psychiatric diagnoses who received psychiatric treatment in a specialized, developmental disabilities–oriented, psychiatric partial hospital setting. Outcomes were contrasted among 3 treatment groups defined by the use of atypical antipsychotic medications. The ABC was used to identify measurable psychiatric symptom response to 3 different antipsychotic medication subgroups in this unique outpatient population. This retrospective study was designed to examine the hypothesis that, for those with mental retardation and coexisting psychiatric symptoms being treated with antipsychotics in this specialized setting, clinical symptom change over time as rated on the ABC would be correlated with the use of antipsychotic medication, and differences in treatment response would be apparent between diagnostic groups.

## METHOD

### Setting

This chart review study examined the medical records of 72 patients consecutively admitted to the psychiatric partial hospital at McLean Hospital's Developmental Dis-

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abilities Program (DDP)[26,27] during the 2-year period from January 1998 to December 1999. All patients were determined to have met criteria for mental retardation prior to the DDP admission, had at least moderate language functioning, and resided in the community. Admission criteria for treatment at the DDP also included a current episode of acute psychiatric illness. Thus, the majority of patients were already involved in psychiatric treatment and were taking psychotropic medications, particularly the antipsychotic agents, at the time of admission to the DDP.

As this study was retrospective in nature, it should be noted that medication treatment decisions at the DDP were made clinically and entirely without regard to any intent to study this patient sample. Thus, medication treatment was managed individually, in accordance with each patient's clinical situation. At the DDP, patients were admitted with acute changes in mental status and generally discharged to the community in improved condition following psychopharmacologic, psychosocial, and cognitive-behavioral interventions. Those subjects whose condition deteriorated in the partial hospital level of care were discharged to a more restrictive setting such as a locked psychiatric inpatient unit. ABC scores, Global Assessment of Functioning (GAF)[28] ratings, and psychotropic medication data were available in the DDP medical record regardless of venue at discharge. Thus, the intent-to-treat sample for this study included all patients who were admitted to the partial hospital regardless of length of stay or condition at discharge. All antipsychotic dose data obtained from the medical records were transformed to chlorpromazine equivalents.[29]

### Demographics

The patient sample and research methods have been described in a previous report[30] and will only be briefly reviewed here. All chart review data including patient demographics, diagnoses, medication information, and scores on the ABC and GAF scales at admission and discharge were collected from the medical records by one of the authors (C.M.). All patients had been treated by the same psychiatrist (K.J.S.), who made clinical, DSM-IV–based diagnoses and served as the patients' treating physician during the treatment period.

Psychiatric diagnoses were made using data from available records, patient interviews, and information given by informants who knew the patients well. Rating scale scores for both the ABC and GAF, also generated during the DDP admission and by the clinical team treating the patient at the time, were determined by consensus of 1 of 2 clinical teams, such that each patient was rated by either one or the other of the teams. Because of the nature of the clinical program, raters had not been blinded to patient identity when generating rating scale scores.

Antipsychotic medication use and primary diagnostic category data were based on information recorded in medical records at the time of discharge from the DDP. For each subject, all psychotropic medications were identified. Three antipsychotic medication use categories were defined: (1) no antipsychotic (antipsychotics—none subgroup), (2) atypical antipsychotic only (atypical-only subgroup), and (3) typical antipsychotic only or mixed atypical/typical antipsychotics (typical/mixed subgroup). For the purposes of this study, 5 diagnosis categories were defined: bipolar disorder; major depressive disorder (MDD) without psychosis; MDD with psychosis; schizophrenia spectrum disorders (including schizophrenia, schizoaffective disorder, schizophreniform disorder, and psychotic disorder not otherwise specified [NOS]); and impulse control disorder. Patients diagnosed with psychotic disorder NOS or schizoaffective disorder were included in the schizophrenia spectrum disorders category due to the distinct and persistent presence of psychotic features in these individuals. It was felt that the density of psychotic features required for these diagnoses most closely allied these subjects to those with schizophrenia rather than to those with distinct, episodic mood disorders that were characterized by the resolution of both the mood and psychotic features during periods of stability.

### Measures

The GAF is a well-known, ordered rating scale that assigns a score from 1 to 100 representing the severity of illness at a single point in time in accordance with clinical features including the presence or absence of psychiatric symptoms, the level of social and occupational functioning, and the degree of impairment in self-care. The ABC instrument is made up of 5 separate subscales: (1) irritability, (2) social withdrawal, (3) stereotypy, (4) hyperactivity, and (5) inappropriate speech.[24] Each ABC subscale comprises multiple statements providing detailed behavioral descriptions of observable features. Ratings from 0 for "not at all" to 3 for "always" or "severe" are generated for each behavioral item. Scores on each ABC subscale are the composite of the items associated with each category. In addition to the GAF and ABC ratings, an overall summary rating of each patient's clinical status at discharge was made by staff consensus, with 1 of 3 status levels assigned for each patient: improved, unchanged, or deteriorated.

### Statistical Analyses

All computational analyses were carried out by a blinded psychometrician who was not part of the clinical team (J.H.). Associations between ABC subscales, baseline demographic variables, and antipsychotic medication subgroup were assessed using logistic regression modeling methods. Study data were assembled in panel format, that is, 2 records per patient, with one record for baseline data (admission) and a second record for endpoint data (discharge). Random effects regression modeling meth-

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**Table 1. Sample Description/Baseline Measures of Adults With Mild Mental Retardation and Comorbid Psychiatric Disorders by Antipsychotic Medication Treatment**

| Characteristic | Antipsychotic Medication | | | $\chi^2$ or t[b] | p |
|---|---|---|---|---|---|
| | None | Atypical Only | Typical/Mixed[a] | | |
| Subjects, N (%) | 15 (20.8) | 41 (56.9) | 16 (22.2) | | |
| Female, N (%) | 13 (36.1) | 17 (47.2) | 6 (16.7) | 10.4 | .005 |
| Age at hospital admission, mean ± SD, y | 35.9 ± 10.9 | 36.2 ± 9.6 | 41.1 ± 10.0 | 1.40 | .17 |
| GAF score at admission, mean ± SD | 37.2 ± 4.6 | 35.1 ± 5.7 | 37.0 ± 5.8 | 0.08 | .93 |
| Length of hospital stay, mean ± SD (median), d | 108 ± 94 (65) | 146 ± 112 (104) | 141 ± 137 (117) | 0.65 | .52 |
| Diagnostic category, N (%)[e] | | | | | |
| Bipolar disorder | 4 (27) | 5 (12) | 1 (6) | | .26 |
| MDD without psychosis | 7 (47) | 4 (10) | 0 (0) | | .001 |
| MDD with psychosis | 3 (20) | 9 (22) | 4 (25) | | 1.00 |
| Schizophrenia spectrum[c] | 0 (0) | 20 (49) | 10 (63) | | < .001 |
| Impulse control disorder | 1 (7) | 3 (7) | 1 (6) | | 1.0 |
| Other medications, N (%)[d,e] | 14 (93) | 37 (90) | 16 (100) | | .70 |

[a]"Typical/Mixed" indicates typical antipsychotic only or atypical plus typical antipsychotic combination.
[b]Summary statistics are $\chi^2$ (df = 2) for nominal data and t (df = 69) for continuous measures. Fisher exact test was used for categorical tables with cell counts ≤ 5.
[c]"Schizophrenia spectrum" includes schizophrenia, schizoaffective disorder, schizophreniform disorder, and psychosis not otherwise specified.
[d]"Other medications" indicates the number of subjects prescribed 1 or more antidepressants, antianxiety agents, mood stabilizers, antiadrenergics, or antiparkinson drugs.
[e]p Values represent Fisher exact test.
Abbreviations: GAF = Global Assessment of Functioning, MDD = major depressive disorder.

ods assessing the roles of atypical antipsychotic medication and time and controlling for clinically important covariates (gender, age, diagnosis, and baseline GAF score) were used in analyses of ABC subscale data.[31] Some associations between ABC subscale change-from-baseline and GAF change-from-baseline scores were assessed using Spearman rank-based correlation methods.

In the random effects modeling work, the random effects were the subjects, and the fixed effects were atypical antipsychotic subgroup, time, and the several covariates of interest. These models contrasted treatment outcomes (GAF and ABC subscales change-from-baseline scores) among the 3 antipsychotic medication subgroups, with adjustment as appropriate for important covariates. Model fits were checked by examining partial residual plots.

Averaged continuous data are reported as means with standard deviations (± SD) or means with 95% confidence intervals (95% CIs), except for length-of-stay data, for which both medians and means ± SDs are reported because of prominent positive skewness. For categorical data, $\chi^2$ methods with appropriate degrees of freedom (df) were used, except that Fisher exact test was used for tables with cell sizes ≤ 5. Statistical significance required 2-tailed $p < .05$. Analyses employed Stata[32] software.

## RESULTS

### Characteristics of the Study Sample

Baseline and endpoint data were obtained for 72 subjects (100%). Among the 72 subjects, there were 36 women and 36 men. The patients ranged in age from 19 to 62 years (mean = 37.2 ± 10.0 years) and were diagnosed with mild mental retardation (96%, N = 69) or borderline intellectual functioning (4%, N = 3). The mean number of psychotropic medications of all types at the time of admission for this group was 2.93 (range, 0–7). Of these, 57 of the 72 patients were prescribed an antipsychotic at the time of discharge from the DDP, while 15 patients were treated with no antipsychotic at discharge. Of those receiving an antipsychotic at discharge, 41 patients were receiving atypical antipsychotics alone, 5 patients were receiving typical antipsychotics alone, and 11 patients were receiving the combination of typical plus atypical antipsychotic treatment.

During treatment at the DDP, 17 (41%) of 41 patients receiving atypical antipsychotics alone had their doses increased, while 24 (59%) of 41 doses were unchanged. For those receiving combination treatment, all received increased doses during DDP treatment. Characteristics of the sample of 72 patients, aggregated separately for the 3 antipsychotic treatment subgroups (antipsychotics—none [N = 15], atypical-only [N = 41], and typical/mixed [N = 16]) are summarized in Table 1. At the time that these study data were obtained, 4 atypical antipsychotics were available in the United States and comprised the following proportions of this sample: clozapine (4/58, 7%), risperidone (19/58, 33%), olanzapine (25/58, 43%), and quetiapine (10/58, 17%). Six of 41 subjects in the atypical-only group received 2 simultaneous atypical antipsychotics, while 11/16 subjects in the typical/mixed group received an atypical along with a typical antipsychotic.

The 72 subjects were equally divided by gender; however, proportionally more women (13 of 15, 87%) were in the antipsychotics—none group than in the atypical-only

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**Table 2. Aberrant Behavior Checklist (ABC) Subscales and Global Assessment of Functioning (GAF) Baseline and Change-From-Baseline Scores in Adults With Mild Mental Retardation and Comorbid Psychiatric Disorders by Antipsychotic Medication Treatment**

| | Antipsychotic Medication | | | Statistic | |
|---|---|---|---|---|---|
| Characteristic | None (N = 15) | Atypical Only (N = 41) | Typical/Mixed (N = 16) | F[a] | p |
| Baseline score, mean ± SD | | | | | |
| ABC subscale | | | | | |
| Irritability | 19.5 ± 11.0 | 13.3 ± 10.4 | 15.3 ± 9.2 | 1.82 | .17 |
| Social withdrawal | 4.3 ± 5.8 | 10.9 ± 10.6 | 7.9 ± 7.8 | 4.42 | .016 |
| Stereotypy | 2.6 ± 5.3 | 2.2 ± 4.4 | 3.6 ± 5.1 | 0.46 | .63 |
| Hyperactivity | 19.5 ± 10.4 | 15.8 ± 11.6 | 12.8 ± 9.8 | 1.72 | .19 |
| Inappropriate speech | 2.8 ± 3.5 | 3.1 ± 3.5 | 2.4 ± 3.2 | 0.22 | .80 |
| GAF total | 37.2 ± 4.6 | 35.1 ± 5.7 | 37.0 ± 5.8 | 1.28 | .28 |
| Change in score from baseline, mean ± SD | | | | z[b] | p |
| ABC subscale | | | | | |
| Irritability | –10.8 ± 11.6 | –6.7 ± 8.2 | –8.4 ± 10.3 | 0.78 | .44 |
| Social withdrawal | –2.8 ± 6.3 | –5.8 ± 8.3 | –4.1 ± 4.8 | –3.40 | .001 |
| Stereotypy | –2.0 ± 4.1 | –0.45 ± 3.7 | –1.9 ± 4.9 | 1.90 | .057 |
| Hyperactivity | –9.3 ± 12.2 | –7.8 ± 9.9 | –5.8 ± 10.0 | 0.27 | .78 |
| Inappropriate speech | –1.7 ± 3.4 | –1.3 ± 3.0 | –1.2 ± 2.5 | 1.41 | .16 |
| GAF total | +5.8 ± 6.4 | +8.9 ± 11.2 | +9.5 ± 6.1 | –0.29 | .77 |

[a]For each scale or subscale, the baseline F statistic (df = 2,69) was obtained using regression modeling methods with 2 indicator variables identifying the atypical-only and typical/mixed subgroups as the primary explanatory factors, and with the none subgroup as the comparator.
[b]The change-from-baseline z statistic was obtained using multiple-time-period generalized linear regression methods, with adjustment for clustering within subjects; in these change-from-baseline analyses, the time × atypical-only interaction is the effect for which the summary z statistic is provided.

group (17 of 41, 41%) or the typical/mixed group (only 6 of 16, 38%). This gender × antipsychotic distribution was highly statistically significant ($\chi^2 = 10.4$, df = 2, p = .005; Table 1). There were no significant differences among the 3 treatment groups in age at admission, GAF score at admission, or length of stay at the DDP.

Among 5 diagnostic categories (bipolar disorder; MDD with and without psychotic features; schizophrenia spectrum disorders [including 14 cases of schizoaffective disorder, 8 of schizophrenia, 1 of schizophreniform disorder, and 7 of psychosis NOS]; and impulse control disorder), there were disproportionally fewer subjects treated with antipsychotic medications in the MDD without psychosis category, as expected, and disproportionally more subjects treated with antipsychotic medications in the schizophrenia spectrum disorders category, again as expected (Table 1).

## Clinical Ratings of Patient Improvement

As noted, overall ratings of clinical status (improved, unchanged, or deteriorated) were made at discharge by staff consensus. Among the 72 subjects, 56 (78%) were rated improved, 11 (15%) unchanged, and 5 (7%) deteriorated. Percentages of subjects in these 3 improvement categories did not differ appreciably among the 3 antipsychotic medication subgroups. Among the 56 subjects who were rated as improved, 11/15 (73.3%) were in the antipsychotics—none subgroup, 32/41 (78.0%) in the atypical-only subgroup, and 13/16 (81.3%) in the typical/mixed subgroup ($\chi^2 = 0.28$, df = 1, p = .87). Similarly, of the 5 subjects whose clinical status was rated as deteriorated at discharge, 4/41 (9.8%) were in the atypical-only subgroup and 1/16 (6.3%) was in the typical/mixed subgroup (Fisher exact test; p = .82).

## Baseline and Change-From-Baseline ABC and GAF Data

Admission (baseline) and discharge (change-from-baseline) scores on the 5 ABC subscales and the GAF scale are summarized separately for the 3 antipsychotic medication treatment groups in Table 2.

At baseline, there were no significant differences in score among the 3 antipsychotic medication treatment groups on the GAF measure and on 4 of the 5 ABC subscales (Table 2). The exceptional ABC subscale, on which baseline values were higher and change-from-baseline scores were larger for the atypical-only subgroup, was the ABC social withdrawal subscale (ABC-2). At baseline, patients receiving atypical antipsychotics alone had much higher ABC-2 scores (indicating greater symptom severity) than subjects in both the antipsychotics—none subgroup and the typical/mixed subgroup. Also, in terms of change from baseline (negative values indicating clinical improvement), patients receiving atypical antipsychotics alone achieved greater improvement in social withdrawal symptoms assessed by the ABC-2 subscale than subjects in both the antipsychotics—none subgroup and the typical/mixed subgroup. When these contrasts were

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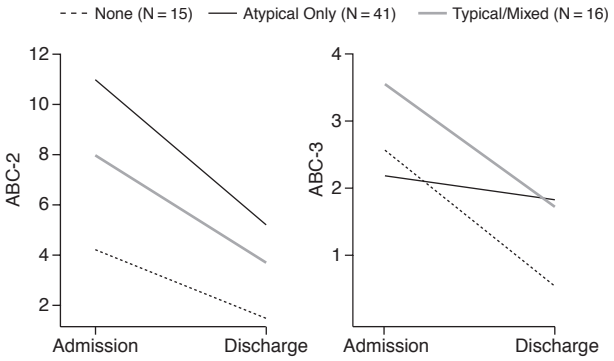
limited to the 62/72 subjects (86%) with baseline ABC-2 subscale scores > 0 (i.e., limited to subjects for whom there was room for improvement in baseline ABC-2 levels), the higher severity levels at baseline and the greater change-from-baseline outcomes of the atypical-only subgroup did not change (data not shown). There was also a trend toward significance in the comparison between the 3 antipsychotic medication subgroups on the stereotypy subscale (ABC-3), with the change-from-baseline scores being less robust for those taking atypical antipsychotics alone than for either of the other 2 medication groups.

Admission and discharge scores on ABC-2 and ABC-3 subscales for the 3 antipsychotic medication subgroups are shown graphically in Figure 1. The figure clearly indicates that subjects in the atypical-only subgroup were both more symptomatic at baseline and achieved greater improvement on the social withdrawal measure than subjects in the other 2 treatment subgroups. This difference was especially pronounced for the atypical-only compared to the antipsychotics—none subgroup. Interestingly, the typical/mixed subjects were intermediate in terms of ABC-2 scores between the atypical-only and antipsychotics—none subgroups, both at baseline and at endpoint (Figure 1, ABC-2). For the stereotypy (ABC-3) measure, subjects in the atypical-only group showed little change over time from admission to discharge, while subjects in the antipsychotics—none and typical/mixed subgroups demonstrated reductions in stereotypies. At admission, subjects in the typical/mixed subgroup had more stereotypies (ABC-3) than those in the atypical-only or antipsychotics—none groups. However, these differences were not statistically significant. At discharge, the ABC-3 scores in the 3 treatment groups did not differ (Figure 1, ABC-3).

**Figure 1. ABC Social Withdrawal (ABC-2) and Stereotypy (ABC-3) Ratings for Adults With Mild Mental Retardation and Comorbid Psychiatric Disorders (N = 72)**




Abbreviation: ABC = Aberrant Behavior Checklist.

### Dose-Response: Antipsychotic Medication Dosage and ABC/GAF Change-From-Baseline Data

There was a substantial dose-response relationship between change from baseline on the ABC-2 (social withdrawal) subscale and endpoint antipsychotic medication dosage level in the atypical-only subgroup, measured in chlorpromazine equivalents. Among the 41 subjects treated with atypical antipsychotics alone, the correlation between ABC-2 change from baseline and endpoint antipsychotic dose level was r = –0.308 (p = .049). This is a negative correlation, indicating that, on average, subjects with higher doses of atypical medications at discharge experienced greater improvement on the ABC-2 (social withdrawal) subscale.

### Sex and Age Differences

There were no statistically significant differences between men and women within the 3 antipsychotic medication subgroups, at admission or at discharge, on the 5 ABC subscales or the GAF. Except for the ABC-4 (hyperactivity) subscale, age was not correlated with ABC subscale scores, across all or within any of the 3 antipsychotic medication subgroups. However, on the ABC-4 (hyperactivity) subscale, age was significantly correlated with both baseline levels (r = –0.26, p = .026) and change from baseline (r = +0.25, p = .036). These age-hyperactivity associations were found almost uniformly across all 3 antipsychotic medication subgroups (data not shown). Younger subjects had higher mean baseline ABC-4 scores (17.7 ± 11.4 vs. 14.0 ± 10.6 for younger vs. older subjects); based on median split on age, this difference was statistically significant (t = 2.35, df = 70, p = .021). Younger subjects also recorded significantly greater mean change (improvement) on the ABC-4 subscale scores (–9.4 ± 8.7 vs. –5.8 ± 11.7; t = 2.42, df = 70, p = .018). The ABC-4 improvement differential associated with subject age was quite substantial; for example, among younger-than-average subjects (defined by median split), the mean ABC-4 change-from-baseline score was –9.4 ± 8.7, compared with –5.8 ± 11.7 among older-than-average subjects. This correlation was found across all 3 antipsychotic medication subgroups.

### Diagnostic Category Differences

As expected, psychiatric diagnoses were differentially clustered among the 3 medication treatment groups, with patients diagnosed with MDD without psychosis comprising a relatively large proportion of the group receiving no antipsychotics, while patients diagnosed with schizophrenia spectrum disorders and bipolar disorder were overrepresented in the 2 groups receiving treatment with antipsychotics. In the antipsychotics—none subgroup, 10/15 (67%) of the subjects had a primary diagnosis of MDD; in the antipsychotic medication subgroups (atypical-only and typical/mixed), 36/57 (63%) of the subjects were either schizophrenia spectrum disorder or bipolar disorder patients.

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**Table 3. Outcomes: Mean Change in Score From Baseline on the Aberrant Behavior Checklist (ABC) Subscales[a] and Global Assessment of Functioning (GAF) in Adults With Mild Mental Retardation and Comorbid Psychiatric Disorders by Diagnostic Category**

| | Antipsychotic Medication | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | None | | Atypical Only | | Typical/Mixed | | | |
| Scale | Mean Change ± SD | N | Mean Change ± SD | N | Mean Change ± SD | N | z[c] | p |
| ABC-1 | | | | | | | | |
| Bipolar disorder | –8.5 ± 16.1 | 4 | –10.0 ± 12.4 | 5 | –14.0 ± NA[b] | 1 | 0.05 | .96 |
| MDD without psychosis | –16.9 ± 9.2 | 7 | –8.0 ± 7.4 | 4 | NA | 0 | –1.85 | .064 |
| MDD with psychosis | –0.7 ± 2.3 | 3 | –4.1 ± 5.7 | 9 | –5.7 ± 10.7 | 4 | 0.16 | .88 |
| Schizophrenia spectrum disorder | NA | 0 | –6.9 ± 8.6 | 20 | –9.1 ± 11.5 | 10 | –0.54 | .59 |
| ABC-2 | | | | | | | | |
| Bipolar disorder | –5.5 ± 7.1 | 4 | –1.6 ± 4.2 | 5 | 0.0 ± NA[b] | 1 | –0.81 | .42 |
| MDD without psychosis | –3.3 ± 6.5 | 7 | –6.8 ± 3.3 | 4 | NA | 0 | 1.22 | .22 |
| MDD with psychosis | 1.3 ± 4.0 | 3 | –8.7 ± 9.4 | 9 | –2.8 ± 2.2 | 4 | 2.31 | .021 |
| Schizophrenia spectrum disorder | NA | 0 | –6.4 ± 8.9 | 20 | –5.3 ± 5.7 | 10 | 0.44 | .66 |
| ABC-3 | | | | | | | | |
| Bipolar disorder | –1.8 ± 3.5 | 4 | –0.4 ± 0.9 | 5 | 0.0 ± NA[b] | 1 | –0.73 | .47 |
| MDD without psychosis | –2.0 ± 5.3 | 7 | –0.5 ± 2.5 | 4 | NA | 0 | –0.67 | .51 |
| MDD with psychosis | –2.3 ± 4.0 | 3 | +0.1 ± 3.8 | 9 | +0.8 ± 4.3 | 4 | –0.35 | .73 |
| Schizophrenia spectrum disorder | NA | 0 | –0.7 ± 4.6 | 20 | –3.4 ± 5.1 | 10 | –1.44 | .15 |
| ABC-4 | | | | | | | | |
| Bipolar disorder | –13.7 ± 16.3 | 4 | –13.2 ± 10.6 | 5 | +8.0 ± NA[b] | 1 | 0.45 | .65 |
| MDD without psychosis | –13.3 ± 6.8 | 7 | –5.0 ± 4.4 | 4 | NA | 0 | –2.58 | .010 |
| MDD with psychosis | +7.0 ± 1.7 | 3 | –3.9 ± 7.8 | 9 | –4.0 ± 9.0 | 4 | 1.14 | .25 |
| Schizophrenia spectrum disorder | NA | 0 | –8.2 ± 11.6 | 20 | –7.4 ± 10.5 | 10 | 0.21 | .84 |
| ABC-5 | | | | | | | | |
| Bipolar disorder | –3.2 ± 4.6 | 4 | –1.4 ± 2.2 | 5 | –3.0 ± NA[b] | 1 | –0.94 | .35 |
| MDD without psychosis | –1.4 ± 2.5 | 7 | –1.2 ± 3.2 | 4 | NA | 0 | –0.10 | .92 |
| MDD with psychosis | +1.3 ± 0.6 | 3 | –0.6 ± 2.6 | 9 | 0.0 ± 1.6 | 4 | 1.14 | .25 |
| Schizophrenia spectrum disorder | NA | 0 | –1.6 ± 3.6 | 20 | –1.8 ± 2.7 | 10 | –0.13 | .90 |
| GAF | | | | | | | | |
| Bipolar disorder | +3.2 ± 2.4 | 4 | +18.2 ± 9.9 | 5 | +15.0 ± NA[b] | 1 | 2.62 | .009 |
| MDD without psychosis | +9.1 ± 4.7 | 7 | –0.3 ± 11.4 | 4 | NA | 0 | –1.73 | .084 |
| MDD with psychosis | 0.0 ± 10.0 | 3 | +7.9 ± 11.3 | 9 | +10.7 ± 8.1 | 4 | –0.34 | .73 |
| Schizophrenia spectrum disorder | NA | 0 | +9.3 ± 10.7 | 20 | +9.6 ± 4.3 | 10 | –0.14 | .89 |

[a]ABC subscales: ABC-1, irritability; ABC-2, social withdrawal; ABC-3, stereotypy; ABC-4, hyperactivity; ABC-5, inappropriate speech.
[b]For N = 1 subgroups, SD cannot be calculated.
[c]For each scale, the z statistics assess change-from-baseline differences for atypical antipsychotics vs. other treatments.
Abbreviations: MDD = major depressive disorder, NA = not applicable.

For the purposes of summarizing ABC and GAF data by diagnosis for each of the 3 medication subgroups, we formed 4 categories by excluding from the statistical analysis the 5 patients who were diagnosed with impulse control disorder (Table 3). We believe that this exclusion is appropriate because the impulse control disorder designation is a nonspecific entity that also may lack psychiatric diagnostic validity. The resulting 4 categories were bipolar disorder (N = 10), MDD without psychosis (N = 11), MDD with psychosis (N = 16), and schizophrenia spectrum disorders (N = 30).

Baseline GAF scores did not differ significantly among the 4 diagnostic categories (data not shown). In contrast, as expected, baseline ABC subscale scores differed substantively among the 4 diagnostic categories at baseline in several specific areas. There was a differential split for patients in the MDD diagnostic subgroup on baseline ABC measures between those diagnosed with MDD without psychosis and those diagnosed with MDD with psychosis. Subjects in the MDD without psychosis diagnostic category had significantly lower scores than other subjects on the ABC-5 (inappropriate speech) subscale at baseline (1.7 ± 2.3 for MDD without psychosis vs. 3.1 ± 3.5 for all others, z = 2.37, p = .019).

Subjects diagnosed with MDD with psychosis were significantly different from the other subjects at baseline on 3 of the ABC subscales: (1) On the ABC-1 (irritability), these subjects scored significantly lower than average at baseline (10.9 ± 8.4 for MDD with psychosis vs. 16.2 ± 10.8 for all others, z = 2.97, p = .004). (2) On the ABC-4 (hyperactivity), these subjects scored significantly lower than average at baseline (9.1 ± 9.0 for MDD with psychosis vs. 17.8 ± 10.9 for all others, z = 4.68, p < .001). (3) On the ABC-5 (inappropriate speech), these subjects scored significantly lower than average at baseline (1.7 ± 3.1 for MDD with psychosis vs. 3.2 ± 3.4 for all others, z = 2.33, p = .021).

Subjects in the bipolar disorder diagnostic category were also significantly different from the other subjects on 3 of the ABC subscales at baseline: (1) On the ABC-2 (social withdrawal), these subjects scored significantly lower than average (4.0 ± 5.5 for bipolar vs. 9.7 ± 9.8 for

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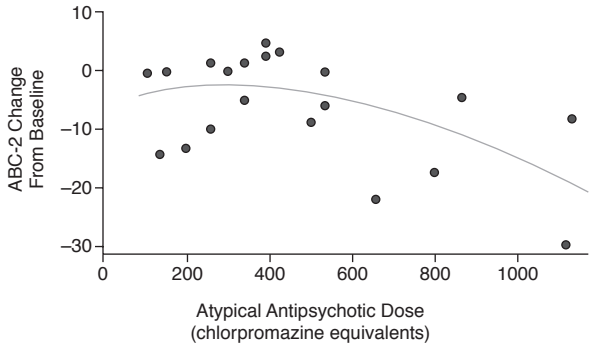
Figure 2. ABC Social Withdrawal (ABC-2) Ratings for Adults With Mild Mental Retardation and Comorbid Schizophrenia Spectrum Disorder (N = 30)




Abbreviation: ABC = Aberrant Behavior Checklist.

all others, z = 3.86, p < .001). (2) On the ABC-3 (stereotypy), these subjects scored significantly lower than average at baseline (0.9 ± 2.2 for bipolar vs. 2.9 ± 4.7 for all others, z = 3.10, p = .004). (3) On the ABC-5 (inappropriate speech), these subjects scored significantly higher than average at baseline (5.3 ± 4.3 for bipolar subjects vs. 2.5 ± 3.1 for all others, z = 2.91, p = .004). In contrast, as subjects in the schizophrenia spectrum disorder diagnostic subcategory fell into only 2 of the 3 medication treatment subgroups (the active antipsychotics subgroups), there were no noted differences between medication treatment subgroups for these patients.

Change-from-baseline differences on the 5 ABC subscales and the GAF scale are summarized separately in Table 3 for each of the 3 medication treatment subgroups. These analyses were limited by small and unequal cell sizes, and there were several empty cells based on the diagnosis × antipsychotic medication subgroup matrix. There were 3 contrasts in which there were statistically significant differences in change from baseline in this ABC subscale × diagnostic category × atypical antipsychotic subgroup matrix (Table 3). For the ABC-2 (social withdrawal), subjects with psychotic depression achieved higher-than-average changes (improvements) in the atypical-only medication subgroup at endpoint. For the ABC-4 (hyperactivity), subjects diagnosed with nonpsychotic depression recorded greater-than-average improvement in the antipsychotics—none medication subgroup at endpoint. On the GAF, subjects with bipolar disorder achieved significantly greater improvement in both the atypical and typical/mixed subgroups at endpoint (Table 3).

In addition, there were 2 statistical trends involving patients diagnosed with nonpsychotic depression who took no antipsychotics. This group improved on the ABC-1 (irritability) subscale and the GAF (Table 3). There were no statistical differences in improvement on ABC subscales or the GAF between the antipsychotic medication subgroups for patients diagnosed with schizophrenia spectrum disorders (Table 3). As noted above, in contrast to those subjects diagnosed with mood disorders, subjects in the schizophrenia spectrum disorder diagnostic subcategory fell into only 2 of the 3 medication treatment subgroups. Thus, as expected, on change-from-baseline comparisons between these 2 active antipsychotic treatments within the schizophrenia spectrum disorder diagnostic subcategory, there were essentially no differences.

### Dose-Response: Antipsychotic Medication Dosage and Diagnostic Category

As noted above, a substantial dose-response relationship between change from baseline on the ABC-2 (social withdrawal) subscale and atypical antipsychotic medication dose level at discharge was found within the atypical-only subgroup. When breaking down this correlation by diagnostic subcategory, it was found that this correlation (r = –0.308, p = .049) was due almost entirely to the dose-response association within the schizophrenia spectrum subgroup. In this subgroup, where the antipsychotic medication presumably was likely to have a large effect (N = 20), the correlation between antipsychotic dosage at discharge and ABC-2 change from baseline was very strong (r = –0.486, p = .030). In contrast, for the bipolar disorder and MDD diagnostic categories, within which only a few subjects were treated with atypical antipsychotic drugs, these correlations were near zero (for bipolar disorder patients, r = +0.11, p = .86; N = 5; MDD with and without psychosis patients, r = –0.16, p = .60; N = 13).

The strong correlation between improvement on the ABC-2 (social withdrawal) subscale over baseline levels and atypical antipsychotic dose at discharge is shown graphically in Figure 2. Of note, the figure suggests that almost all of this correlation is due to the strength of this association among subjects with relatively high levels of medication dose at discharge. Neither the GAF nor any of the other 4 ABC subscales was found to be correlated with atypical antipsychotic dose.

### Other Psychotropic Medications

Other psychotropic medications prescribed at least once during the study period included benzodiazepine anxiolytics (31/72, 43.1%), antidepressants (43/72, 59.7%), mood stabilizers (34/72, 47.2%), anti-adrenergic and antiparkinsonian agents (43/72, 59.7%), and buspirone (5/72, 6.9%). None of these drugs were found to be correlated with positive (or negative) response to treatment within any of the diagnostic subgroups (data not shown).

## DISCUSSION

Clinical symptom improvement in dually diagnosed patients with mild mental retardation and coexisting psy-

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chotic illness treated in a specialized partial hospital setting was associated with the use of antipsychotic medications. While there were no differences in overall level of mental retardation or psychiatric illness among subjects in the 3 medication treatment groups at admission, there were marked differences in symptom presentation and responses between medication treatment groups as measured by the ABC instrument. In this community sample, it is striking that (1) such complex patients can demonstrate improvement over the course of treatment on any features measured by rating scales and (2) there would be any association between medication dose within a particular class of psychotropics and diagnosis-associated improvements on these measures.

The ABC instrument, the most widely used assessment scale for rating observable change during pharmacologic treatment in the mental retardation/developmental disability population, is heavily weighted toward behaviors that occur in moderate to severe mental retardation and in institutional settings. While not developed for our population of relatively higher-functioning psychiatric outpatients, the ABC has been used in other outpatient settings as an assessment tool in older adults without mental retardation[33] and in a community sample of special-needs schoolchildren.[34]

The issue of psychiatric diagnosis in those with mental retardation/developmental disability has remained elusive, as the focus of medication treatment has often been to reduce symptoms such as self-injurious behaviors, disinhibition, intrusiveness, and hyperactivity without regard to formal psychiatric diagnosis. However, in examining baseline data compiled from the ABC ratings at DDP admission for this patient sample, a number of distinct symptom complexes emerged that were felt to be consistent with our clinical diagnostic experience in dual diagnosis. Patients with both psychotic depression and schizophrenia spectrum disorders presented as withdrawn and preoccupied, while those with nonpsychotic depression presented as irritable and those with bipolar disorder were motorically hyperactive and inappropriately talkative. In addition, younger patients, regardless of diagnosis, were more active at baseline than were older patients in this sample. These observations are, in fact, consistent with clinical experience in similar treatment settings for individuals diagnosed with mental illness who are not affected by intellectual disability. These findings not only confirm our clinical impressions of the presence of distinct psychiatric diagnoses in this specialty population, but also support the notion that valid psychiatric diagnosis in those with mild mental retardation is less dissimilar to that of the general psychiatric population than might be expected.[35]

While this study is limited by the fact that it did not employ a no-treatment control group for subjects with psychotic diagnoses and did not assign matched subjects to different treatment groups, the inclusion of a no-antipsychotic medication group that was essentially equivalent to the antipsychotic-treated subgroups in level of mental retardation, severity of psychiatric illness as measured by the GAF at admission and discharge, condition at discharge, length of stay, and use of other psychotropic medications permitted comparisons for the effects of active partial hospital treatment across the range of symptoms assessed by the ABC instrument. The data suggest that significant differences on ABC measures were not due to floor effects in patients in the no-antipsychotic group. Significantly elevated social withdrawal (ABC-2) ratings at admission and following treatment were noted only for those patients receiving antipsychotic medications. In fact, these ratings were elevated at admission and remained elevated at the completion of treatment for both of the antipsychotic treatment groups as compared with the group of patients who did not receive antipsychotics. The line graphs of the ABC-2 in Figure 1 clearly indicate that the magnitude of change was greatest for those treated with atypical antipsychotics. The data suggest that this finding was not likely to be attributable to the sedative or anxiolytic effects of the atypical antipsychotics, as ratings for irritability (ABC-1) and hyperactivity (ABC-4) were substantial and did not change to any greater proportion in the atypical-only group during partial hospitalization.

We propose that social withdrawal in this sample may be an indicator of active psychosis, as social withdrawal was so markedly improved in the patients with psychotic depression who were treated with antipsychotic medication, in contrast to those in the nonpsychotic depression and bipolar categories. Presumably, for those in the latter diagnostic categories, treatment with antidepressants and mood stabilizers would be associated with symptom resolution. In addition, for those with schizophrenia spectrum disorders, there was equivalent and substantial improvement in social withdrawal for both of the active antipsychotic treatment subgroups. These findings suggest that some portion of the reduction in social withdrawal symptoms experienced by those who were treated with atypical antipsychotics may be due to at least 2 factors: (1) a reduction in the "negative" symptoms of schizophrenia[36] that has been reported in those treated with the atypicals; and (2) a decrease in "positive" symptoms,[37] or preoccupation with hallucinations and delusions, in those suffering from psychotic syndromes when their psychosis is recognized and treated.

This presumption is supported by the finding that for patients in this sample, the magnitude of improvement in social withdrawal during treatment with atypical antipsychotics was correlated with the dose of atypical antipsychotic at discharge, with the most pronounced improvement being achieved in those patients receiving higher chlorpromazine-equivalent doses. As noted, the

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bulk of this dose-response correlation was due to those diagnosed with schizophrenia spectrum disorders. As social withdrawal ratings for this group remained measurable and non-zero at discharge, the antipsychotic dose/ABC social withdrawal change-from-baseline correlation is not explained by factors such as familiarity with the partial hospital setting over time or complete resolution of symptoms in those patients treated with the atypical agents.

Few conclusions can be drawn from this study regarding those patients who were treated with typical antipsychotic medications. While these subjects were essentially equivalent to the subjects in the other treatment groups in severity of psychiatric illness, age, length of stay, and degree of mental retardation, the number of these subjects was small. Moreover, the fact that they were continued on the older antipsychotics when the trend was to replace these with the novel agents may indicate that this group was distinct from the others on several unmeasured characteristics. Although these individuals carried the diagnosis of "mild" mental retardation, this diagnosis was made in the community, and individual IQ scores were not available for this study. It is possible that these subjects were more intellectually impaired than those in other treatment groups. In addition, it is likely that those individuals who were continued on typical antipsychotics had greater density of behavioral problems or longer duration of psychiatric illness than others in this sample.

The issue of medication side effects in individuals receiving either typical or atypical antipsychotic medication is controversial in those with mental retardation, as the presence of muscle tone abnormalities and stereotypies including tics, mannerisms, and self-stimulatory behaviors can all mask the presence of antipsychotic-induced movement disorders. The presence of any movement disorder or mannerism in these patients can make diagnosis, observation over time, and treatment of the motor condition a puzzle. The finding that stereotypies were reduced during partial hospital treatment in the patients receiving no antipsychotics and in subjects in the typical/mixed antipsychotics group as compared with no reduction in this measure for those in the atypical antipsychotics group is interesting in that in general, for those with developmental disabilities, stereotypies can be intensified in conditions of anxiety or stress and reduced during periods of stability. The persistence of stereotypy in those subjects treated with atypical antipsychotics in this study, at a greater level than for those who are not treated with any antipsychotics, may suggest that antipsychotic-associated movement disorders are present to a similar extent as with the typical antipsychotics in this population. The convergence of the stereotypy ratings at endpoint for both antipsychotic-treated groups, as noted for the ABC-3 in Figure 1, may be a reminder of the importance of this side effect.

Our report of significant associations between the use of atypical antipsychotic medication and improvement in psychiatric symptoms among patients with co-occurring intellectual disability and psychotic illness is potentially important in that social withdrawal is often a constitutional feature of mental retardation and can easily go unrecognized as a treatable complex of negative symptoms associated with schizophrenia or positive symptoms associated with psychotic states. Among those with developmental disability, isolation and introversion may be mistaken for meekness or lack of sophistication rather than indications of preoccupation due to psychosis.

While the atypical antipsychotics are touted as preferred agents for the reduction of negative symptoms, we know of no other reports in the literature in which this outcome might be observed in the dually diagnosed. Thus, the challenge of identifying the underlying etiology of behavioral features in this specialized population is underscored. Though our study was limited by its naturalistic design and lack of traditional psychiatric instruments, our findings suggest that careful, detailed, and multidimensional observation and assessment together with appropriate atypical antipsychotic treatment can lead to notable clinical improvement in patients previously thought to be dually untreatable by virtue of their dual psychiatric and mental retardation diagnoses.

*Drug names:* buspirone (BuSpar and others), chlorpromazine (Thorazine, Sonazine, and others), clozapine (Clozaril, Fazaclo, and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal).

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