Published in final edited form as:

J Clin Psychopharmacol. 2006 August ; 26(4): 419–425. doi:10.1097/01.jcp.0000227356.31203.8a.

Pharmacotherapy and Postdischarge Outcomes of Child Inpatients Admitted for Aggressive Behavior

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Abstract

Objectives—(1) To ascertain the utilization rates of specific pharmacotherapy strategies for child psychiatric inpatients with aggressive behavior from preadmission care through 12 months after discharge, and (2) To examine the associations between these strategies and postdischarge outcomes.

Method—Prospective follow-up of eighty-three 5- to 13-year-old children admitted to acute inpatient care for aggressive behavior in the context of a disruptive behavior disorder. Treatment and symptom severity data were obtained at admission, discharge, and 3, 6, and 12 months after discharge between 1998 and 2001.

Utilization: The number of concurrent medications increased over assessment times. Changes in children's pharmacotherapy occurred most frequently during hospitalization and from discharge to 3 months after discharge. Treatment with antipsychotics and mood stabilizers increased over assessment times, whereas selective serotonin reuptake inhibitor (SSRI) treatment decreased.

Outcomes: Children treated with stimulants and risperidone 3 months after discharge had significantly improved behavioral ratings, adjusted for admission scores utilization and concurrent medications. Children treated with SSRIs at 6 months after discharge had higher problem severity ratings. Those who maintained lithium and SSRI treatment between 6 and 12 months showed improvements.

Conclusions—The complexity of pharmacotherapy for child inpatients ratchets upwards from admission through 1 year after discharge. Hospital-initiated treatment is commonly altered soon after discharge. Within the limitations of observational methodology, their postdischarge outcomes seem related to specific pharmacotherapy regimens.

Controlled studies have indicated the efficacy of several agents for both “classical” psychiatric disorders of childhood and for the early onset of conditions that more typically first manifest in adulthood. However, the available data offer little guidance for the treatment of children who are not robust responders to monotherapy with the agents studied. One patient group at risk for inadequate response to monotherapy with evidence-based treatment comprises youngsters with severe conduct problems that include impulsive aggression. Youth with these difficulties most often meet diagnostic criteria for a disruptive disorder (oppositional defiant or conduct disorder¹). Disruptive disorders are highly comorbid with attention-deficit/hyperactivity disorder (ADHD).^{2,3}

Medication to ameliorate ADHD often reduces disruptive disorder symptoms,^{4–7} but incomplete response is common.^{8–10} Therefore, clinicians frequently layer several agents in

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efforts to improve behavioral stability. However, there is no evidence that any medication combination is more beneficial for these patients than monotherapy.^{11–14}

The development of evidence-based treatment sequences for children with impulsive aggressive behavior necessitates controlled studies and confirmation of their pertinence to clinical practice. In the interim, more readily available data can provide useful information on the use and outcomes of pharmacological treatments. These, in turn, can inform the design of controlled studies by highlighting promising agents, sequences, and combinations.

This report presents the treatment patterns and outcomes obtained prospectively for a cohort of children admitted to psychiatric inpatient care with a chief complaint of aggressive behavior. The study's goals were (1) to examine longitudinally pharmacotherapy strategies from preadmission treatment through 3 postdischarge follow-ups, and (2) to analyze children's clinical outcomes in relation to specific pharmacotherapy regimens. On the premise that both affective instability and more generalized problems with impulse control inform the aggressive behavior that typically leads to hospitalization in this patient group, the main hypothesis was that effective pharmacotherapy would include an antimanic compound^{15–17} and stimulant medication.¹⁸

METHODS

Subjects

The sample comprised 83 children, and was derived as follows: One hundred ninety-two children were admitted to a 15-bed acute care psychiatric inpatient service during a 14-month period beginning in 1998. The families of 123 children consented to participate, 20 declined, 20 could not be contacted for recruitment, and 29 children were under the guardianship of foster care agencies that did not provide timely consent. This report considers the subsample of 83 children admitted with a chief complaint of aggression, whose primary diagnosis was a disruptive behavior disorder and who were discharged to reside in the community. We excluded children with other disorders to reduce heterogeneity and potential confounding effects on treatment choice, treatment response, natural course, and outcomes.

Admission diagnoses were determined in case conferences that included at least 2 child and adolescent psychiatrists, applying *DSM-IV* criteria. The diagnoses were derived from structured assessments at admission, which included history taking and semistructured interviews with caregivers and children following a written outline with prompts that queried *DSM-IV* symptoms for specific disorders.

Data Collection Procedures

At admission, the parents or the guardians met with a clinical assistant who helped them to complete a structured psychosocial history that elicited information on the child's current treatment, including medications and previous hospitalizations. At discharge, the inpatient clinical records provided data on the child's pharmacotherapy during hospitalization, demographic factors, health care financing, and length of stay.

Parents furnished information on the child's treatment at 3, 6, and 12 months after discharge via a structured telephone-administered interview, the *Services Utilization Survey* developed for this study.

Parents completed the Child Behavior Checklist¹⁹ (CBCL) at admission and follow-ups. The CBCL provides a global measure of symptom severity (Total Problems), a composite index of depression, anxiety and social withdrawal symptoms (Internalizing), and a measure of conduct problem symptoms (Externalizing). Parents completed the New York Parent Rating Scale for

Disruptive Behavior⁵ (NYPRS). We used the Physical Aggression and Nonphysical Disruptive subscales.

Follow-up assessments began with the Services Utilization Survey administered by telephone. After completing the telephone interview, parents received the CBCL and NYPRS by mail for completion, which were to be returned afterward in a prestamped envelope. Families received \$25 for each follow-up assessment completed.

Data Analyses

Groups of individual medications constituted five medication classes: stimulants (methylphenidate, dextroamphetamine, mixed amphetamine salts), antimanic agents (lithium, divalproex sodium, carbamazepine, gabapentin), atypical antipsychotics (risperidone, olanzapine), conventional antipsychotics (haloperidol, thioridazine, thiothixene), α_2 -agonists (clonidine, guanfacine), and SSRIs.

The number of medications each child received at each assessment yielded categories of 1, 2, and 3+. The Jonckheere-Terpstra test²⁰ evaluated trends in these categories as a linear function of assessment times. The McNemar test for paired proportions²¹ tested specific transitions between categories over time. Logistic regression examined demographic and clinical variables as predictors of the number of medications at each assessment point. Multiple regression analyzed the relationship between medication and outcomes. The predictor set in each analysis included the outcome's admission score, and the child's pharmacotherapy was coded using a dichotomous variable for each of the five medication groups, indicating a presence or absence or a drug from that group in the child's treatment by values of 1 and 0, respectively.

RESULTS

Sample Characteristics

Patients' mean age at admission was 9.37 years (SD, 1.91 years). Boys represented 81% of the sample. One fourth had a previous psychiatric hospitalization. Most (70.3%) resided with biological or adoptive parents, 12.5% resided with grandparents, 11% were in foster care, and 6.2% lived with other relatives. Ethnicity was diverse, with 41% white, 39% African-American, 15% Hispanic, and 5% reporting mixed heritage. Health care financing was from commercial firms for 39.3% of the patients and from Medicaid for 60.7%. Length of stay averaged 23.76 days but was highly skewed (SD, 26); median length of stay was 16 days. Study participants differed from other patients only in the proportion of those in foster care. Among the entire patient group, 22% were in foster care at admission.

By virtue of the inclusion criteria, all subjects had a primary admitting diagnosis of a disruptive behavior disorder, and 95% had comorbid ADHD. In addition, 8% had a comorbid anxiety disorder, 10% pervasive developmental disorder not otherwise specified, and 45% depression not otherwise specified, which generally signified the prominence of irritable affect subsyndromal for a specific mood disorder.

Most children also received psychotherapeutic. The details of treatment and inpatients' recommendation are in another article.²²

Medication Use from Prehospitalization Treatment to Postdischarge Follow-up

Number of Concurrently Used Agents

Prevalence: The Jonckheere-Terpstra test revealed a linear significant decrease in monotherapy from admission (38%) through 12-month follow-up (19%; $J = 14,785$; $P < 0.05$) with monotherapy rates at the 3- and 6-month follow-ups of 30% and 25%, respectively.

Correlates: Children with a previous psychiatric hospitalization were more likely to have received treatment with 3 or more medications (i.e., to fall in 3M+ group) at admission than were patients with no previous admissions (62.5% vs. 37.5%; odds ratio [OR], 6.42; 95% CI, 1.96–20.96; likelihood ratio χ^2 [$G^2(1)$] = 10.150; $P < 0.01$). Other demographic and clinical variables (sex, ethnicity, age, caregiver's relationship to the child, comorbid diagnoses, length of stay, mental health care setting) bore no relation to preadmission pharmacotherapy.

At 3-month follow-up, children with previous hospitalizations (ie, before study enrollment) were still more likely to be in the 3M+ group (OR, 4.08; 95% CI, 1.30–12.78; $G^2(1) = 6.00$, $P = 0.014$).

At 6-month follow-up, higher NYPRS Physical Aggression subscale scores predicted membership in the 3M+ group (OR, 1.11; 95% CI, 1.001–1.25; $G^2(1) = 4.96$, $P < 0.03$).

Shifts in Number of Agents Between Assessment Times

Prevalence: Between admission and discharge, children were more likely to transition into the 3M+ group than out of it (30.2% of those in the 1M and 2M groups at admission vs. 9% who exit the 3M+ group; paired proportions $\chi^2_1 = 2.68$, $P < 0.01$). By 6-month follow-up, there is further significant movement into the 3M+ group (paired proportions $\chi^2_1 = 2.68$, $P < 0.01$). More children entered the 3M+ group between 3 and 12 months after discharge (73.68%) than reduced medications from 3M+ (7.27%).

Correlates: Children who obtained higher ratings of behavioral difficulties at 3-month follow-up were more likely to have experienced a reduction in their number of concurrent medications between discharge and 3-month follow-up. Higher CBCL Externalizing behavior subscale scores 3 months after discharge correlated with a shift from the 3M+ group at discharge to 2 or fewer medications during the discharge to 3-month follow-up interval (OR, 1.10; 95% CI, 1.00–1.21; $G^2(1) = 4.44$, $P < 0.05$).

Specific Regimens and Maneuvers

The prevalence of treatment with stimulants, α_2 -agonists, and bupropion showed little variation over time (Table 1). However, from admission through 12-month follow-up, the rate of treatment with atypical antipsychotics increased significantly ($z_{\text{Trend}} = -2.22$, $P < 0.03$). The rate of treatment with SSRIs decreased significantly over the assessment times ($z_{\text{Trend}} = 2.55$, $P < 0.02$).

Table 2 presents the proportion of patients who experienced specific medication “maneuvers.” By 3 months after discharge, about 30% of patients experienced discontinuation of a medication prescribed during hospitalization, and about 37% started an additional medication. Subsequent postdischarge assessments show reduced rates of starts and discontinuations. Even so, about half of the children experienced changes in their pharmacotherapy during the postdischarge period, most often the start of new medicines.

Postdischarge Outcomes

Outcomes Associated With Principal Medications—As shown in Table 3, children treated with stimulants and risperidone showed significantly larger reductions at 3-month follow-up, relative to admission scores, on measures of overall behavioral difficulty and externalizing behavior symptoms (CBCL Total, NYPRS Physical Aggression, and NYPRS Other Disruptive Behavior scores). These mean differences are adjusted for coadministered medications and admission values of the outcome measure.

Children receiving antimanics at 6-month follow-up received higher ratings, relative to admission, on several measures relative to those not receiving them (higher adjusted CBCL Total, Externalizing and Internalizing scores, NYPRS Total). SSRI treatment also accompanied higher NYPRS Physical Aggression and Nonphysical Disruptive Behavior scores.

However, at 12-month follow-up, children treated with lithium and SSRIs had significantly improved outcomes on the CBCL Externalizing and NYPRS Physical Aggression and Nonphysical Disruptive Behavior subscales relative to other children.

Longitudinal Trends in Treatment and Outcomes

Children who had stimulant treatment at *both* 3- and 6-month follow-ups showed significant improvements relative to their admission scores at 3 months that diminished by 6 months after discharge. Their CBCL Total Problems raw score mean decreased by 20 points at 3 months, but only by 5 points at 6 months. Comparing these children with those who had stimulant treatment at *neither* 3 nor 6 months after discharge revealed a significant group-by-time interaction ($F_{1,28} = 5.30, P = 0.03$), indicating that the non-stimulant-treated group showed improvements that surpassed the stimulant-treated group at 6-month follow-up. Similarly, NYPRS Physical Aggression scores at 3-month follow-up showed a significant 11-point decline from admission ($F_{8,28} = 4.98, P = 0.03$), but the same children at 6-month follow-up showed a 5-point increase. Non-stimulant-treated children had NYPRS Physical Aggression scores that decreased by 3 points, then increased by 1 point, at 3- and 6-month follow-ups, respectively.

Comparing children treated with risperidone at both 3 and 6 months after discharge with children who did not receive risperidone yields similar results. The risperidone-treated patients' CBCL Total Problems score showed a mean decrease from admission of 17 points at 3-month follow-up, compared with a decrease of 3 points among non-risperidone-treated children ($F_{8,37} = 3.36, P = 0.077$). Risperidone-treated patients had an adjusted mean increase of 5 points at 6 months, whereas there was no increase among non-risperidone-treated children. NYPRS Physical Aggression score also showed a comparable reduction from admission at 3-month follow-up for risperidone-treated children, but increases relative to admission at 6-month follow-up. Time-by-group interaction indicates a marginally reliable shift ($F_{8,43} = 3.39, P = 0.07$).

If the association of stimulants and risperidone with better outcomes diminishes with prolonged exposure, children first beginning these treatments between 3 and 6 months after discharge might have better outcomes at 6 months than do youngsters who had continuous treatment since discharge. Partial support for this notion came in comparisons of children who had stimulant treatment at both 3- and 6-month follow-ups with those who had stimulant treatment *only at 6 months*. Patients who received stimulant treatment at both follow-up points had an adjusted mean increase from their admission scores on their 6-month NYPRS Physical Aggression ratings of 4.3 points, which differed significantly from this outcome among those starting stimulant treatment between 3 and 6 months, whose 6-month ratings decreased (mean decline, 4.8 points; $F_{1,26} = 5.57, P = 0.03$). No such effects on 6-month outcomes were evident for risperidone treatment.

Analysis of variance of CBCL Externalizing scores compared children treated with lithium at both 6 and 12 months with children who received lithium at neither time. A significant lithium-by-time interaction ($F_{1,26} = 5.23, P = 0.03$) indicated that lithium-treated children did not show significant advantage on this measure until 12 months after discharge. Both groups showed little change at 6-month follow-up from their admission scores (lithium-treated, 4.66-point adjusted mean increase; non-lithium-treated, 0.19-point decrease); but the lithium group

showed much larger decreases at 12 months (lithium-treated, 26.37-point adjusted mean decrease; non-lithium-treated, 13.29-point decrease). Comparison of these groups' NYPRS Physical Aggression scores yielded similar effects (lithium-by-time interaction: $F_{1,26} = 4.16$, $P = 0.052$; 12.45-point adjusted decrease for continuous lithium treatment vs. 7.39-point decrease for lithium nontreatment).

Likewise, children who had SSRI treatment at both 6 and 12 months showed improvements on CBCL Externalizing behavior ratings only at 12-month follow-up relative to youngsters receiving SSRI treatment at neither time (SSRI-by-time interaction: $F_{1,27} = 4.16$, $P = 0.051$; 24.13-point adjusted decrease for continuous SSRI treatment vs. 15.177-point decrease for SSRI-nontreatment). A comparable effect emerged for NYPRS Physical Aggression at 12 but not at 6 months after discharge (SSRI-by-time interaction: $F_{1,27} = 4.16$, $P = 0.05$; 24.13-point decrease for continuous SSRI treatment vs. 15.17-point decrease for SSRI-nontreatment).

DISCUSSION

Utilization data indicate that, as expected, treatment with multiple psychotropic agents consistently exceeds monotherapy in this patient group. Severity of behavior disorder, particularly aggression, predicts more medications in the postdischarge period. Children who experience multiple admissions also have a higher mean number of concurrent medications.

These longitudinal data provide hitherto unreported perspectives on the treatment of severely impaired children. Within 3 months of discharge, there were substantial changes to patients' hospital-prescribed pharmacotherapy. The high rate of further modifications to treatment after 3 months, with new medications and dosage increases being the most common strategies, suggests that difficulties in managing patient's symptoms effectively, and perhaps the development of tolerance to certain medications, may be major challenges for this group. Flux in pharmacotherapy may reflect high treatment refractoriness in this patient group, poor communication between clinicians, or the vagaries of idiosyncratic prescription practices. Outpatient clinicians may also have come to different diagnostic conclusions, which may account for divergence in pharmacotherapy strategies. Whatever its source, it highlights the gap between the needs of this patient group and our current ability to bring effective treatments to bear in clinical practice.

The progressive reduction in SSRI use over the course of children's treatment can be viewed in light of the current appreciation of the potential for these medications to provoke behavioral *activation* or disinhibition among youth with behavioral disorders or, perhaps, a diathesis for a bipolar disorder.^{23–25} We cannot attribute reduced SSRI use over time in these data, collected between 1999 and 2000, to more recent concerns regarding heightened suicidality among youths treated with SSRIs²⁶ that may have altered the prescription practices. Increased rates of antipsychotic exposure over the course of children's treatment comports with recent reports of their generally greater use in children.²⁷

Significant, independent effects emerged for stimulants and risperidone on behavioral problems at the 3-month follow-up. Benefits for stimulant treatment were expected in light of the high comorbidity of ADHD in this patient population and in light of the extensive research showing that these agents ameliorate conduct problems, including aggression.^{15,18,28}

However, the data suggested that the effects associated with these treatments may attenuate over time, a finding consistent with other recent reports. One study²⁹ double-blindly randomized children with disruptive disorders who experienced good acute response with risperidone to either continuation or placebo substitution. By 6 months, 30% of the children who continued on risperidone experienced relapse. A follow-up of children with ADHD in a large trial involving stimulant treatment also showed diminution of stimulant effectiveness.

³⁰ Further research on the durability of treatment effects for severe conduct disturbances with similar patients and over a similar time period to those studied here would be useful.

Reductions in aggression ratings associated with lithium treatment emerged at the 12-month follow-up, primarily among children who had not showed beneficial effects of lithium at 6 months. Others have reported similarly long latencies in response to antimanic treatment among children in clinical care.³¹ Inferences for the duration of an adequate trial generally come from vigorous titration and frequent monitoring for a fairly motivated cohort of clinical trial participants. Moreover, all positive studies to date for lithium in treating children's conduct problems come from inpatient samples. Outpatient treatment-as-usual typically involves less intensive monitoring and dosage adjustment, which could result in a longer response time than what clinical trial or inpatient data suggest.

At 6-month follow-up, SSRI-treated children had higher behavior problem ratings than did non-SSRI-treated children. As noted previously, many children's SSRI treatment terminated after the 6-month follow-up; yet, children on SSRI treatment at 12 months seemed to show more favorable behavioral ratings. It is therefore possible that children whose conditions do not destabilize with SSRI treatment may show treatment-related improvements later. Better characterization of aggressive children who may respond to SSRI treatment, perhaps those with more prominent anxiety or depressive features, could enable their more optimal use.

To reduce analytic complexity, we did not include dosages or durations of treatment nor assessment of adherence. Omitting this information risks a bias toward diminished treatment effects by including children with therapeutic and subtherapeutic exposures in the same treatment group. Attenuated power to detect treatment effects at adequate exposures might account for some of the no-difference results.

Acknowledgments

Supported by NIH grants R03MH058456 and K23MH64975.

The author thanks the staff of the Child Psychiatry Inpatient Unit at Schneider Children's Hospital, Ariella Levy, Nina Schooler, and Ken Gadow.

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TABLE 1
Proportion of Children Treated With Principal Medication Classes at Assessment Times

Medication Class	Assessment				
	Admission	Discharge	3 Months After Discharge	6 Months After Discharge	12 Months After Discharge
Stimulants	55.4	65.3	54.1	58.7	61.8
Antimanics	32.3	34.7	40.5	44.4	41.8
Atypical antipsychotics	33.9	34.7	41.9	44.4	50.9
SSRIs	30.8	32.0	21.6	20.6	14.6
α_2 -Agonists	21.5	26.7	21.6	23.8	23.6
Bupropion	4.6	12.0	12.2	11.1	9.1
Conventional antipsychotics	6.2	0.0	4.1	3.2	1.8
β -blockers	0.0	0.0	1.4	3.2	1.8
Benzodiazepines	4.6	6.7	6.8	3.2	3.6
Tricyclic antidepressants	3.1	1.3	0.00	3.2	3.6

TABLE 2

Summary of Pharmacotherapy Maneuvers From Hospitalization Through One Year After Discharge

Maneuver	Percentage of Patients			
	Admission to Discharge	Discharge to 3 Months After Discharge	3–6 Months After Discharge	6–12 Months After Discharge
Medication starts	61.2	37.4	20.1	16.3
Medication discontinuations	47.7	30.7	12.6	10.3
Dosage increases	23.1	20.9	21.5	17.8
Dosage decreases	5.9	16.4	12.5	15.5
Medication	17.9	8.2	5.0	5.1
Medication regimen unchanged	21.7	44.7	53.6	46.2

TABLE 3

Adjusted Changes in Postdischarge Outcomes Associated With Medications

Outcomes		Medications											
		Stimulants		Risperidone		Olanzapine		Lithium		VPA		α -Agonists	
		Effect	Test	Effect	Test	Effect	Test	Effect	Test	Effect	Test	Effect	Test
CBCL Total Problems	3 Mos	-23.9 ± 16.4	6.11*	-18.3 ± 16.0	3.74 [†]	-0.93 ± 22.9	0	8.54 ± 17.7	0.66	4.40 ± 24.2	0.09	18.37 ± 19.8	2.46
	6 Mos	10.47 ± 15.5	1.3	4.47 ± 16.0	0.22	7.90 ± 27.0	0.24	15.46 ± 17.9	2.13	51.52 ± 25.1	11.94*	3.56 ± 19.5	0.09
	12 Mos	13.17 ± 19.6	1.31	11.27 ± 19.2	0.99	-19.5 ± 34.5	0.92	-12.3 ± 23.3	0.8	19.45 ± 29.9	1.22	-20.6 ± 22.9	2.33
CBCL Externalizing	3 Mos	-5.10 ± 7.2	1.43	-2.27 ± 7.6	0.26	7.90 ± 11.0	1.46	4.34 ± 8.5	0.75	9.72 ± 11.4	2.07	0.78 ± 9.1	0.02
	6 Mos	2.25 ± 6.6	0.33	2.09 ± 6.7	0.28	4.84 ± 11.3	0.52	4.60 ± 7.6	1.03	15.15 ± 9.3	7.6*	0.77 ± 8.0	0.03
	12 Mos	5.24 ± 8.2	1.18	1.97 ± 7.8	0.19	0.65 ± 14.4	0.01	-12.3 ± 9.2	5.09*	2.85 ± 10.4	0.22	-10.2 ± 9.3	3.44 [‡]
CBCL Internalizing	3 Mos	-1.69 ± 5.7	0.25	-3.46 ± 5.7	1.03	-1.29 ± 8.5	0.07	11.90 ± 6.5	9.54*	5.85 ± 8.8	1.24	5.03 ± 6.9	1.51
	6 Mos	2.05 ± 5.2	0.45	-0.59 ± 5.3	0.04	0.43 ± 9.1	0.01	4.90 ± 6.0	1.91	18.95 ± 7.3	18.92*	-0.72 ± 6.3	0.04
	12 Mos	3.81 ± 6.0	1.16	2.62 ± 5.6	0.63	-5.72 ± 10.4	0.88	-5.96 ± 6.6	2.37	3.21 ± 7.5	0.53	-4.66 ± 6.8	1.36
NYPRS Physical Aggression	3 Mos	-7.94 ± 5.6	5.74*	-7.09 ± 5.8	4.19*	-2.66 ± 8.6	0.27	-6.08 ± 6.6	2.44	-7.30 ± 8.7	2.01	3.26 ± 7.0	0.61
	6 Mos	2.86 ± 3.8	1.6	4.29 ± 3.9	3.47 [‡]	5.31 ± 6.6	1.83	3.33 ± 4.4	1.63	4.72 ± 5.4	2.16	-1.03 ± 4.6	0.14
	12 Mos	0.92 ± 2.7	0.34	-0.27 ± 2.6	0.03	-3.01 ± 5.0	1.06	-4.56 ± 3.0	6.77*	-2.59 ± 3.5	1.56	-1.73 ± 3.1	0.89
NYPRS Nonphysical Disruptive	3 Mos	-46.2 ± 35.3	4.87*	-40.8 ± 36.9	3.47 [‡]	-27.2 ± 54.6	0.7	-30.7 ± 41.4	1.57	-43.0 ± 54.6	1.76	21.42 ± 44.4	0.66
	6 Mos	15.50 ± 21.0	1.54	16.23 ± 21.1	1.68	21.41 ± 36.4	0.98	26.62 ± 24.5	3.35 [‡]	18.15 ± 30.4	1.01	-0.82 ± 25.8	0
	12 Mos	18.60 ± 15.1	4.36*	12.20 ± 14.3	2.1	-2.64 ± 26.4	0.03	-22.3 ± 16.8	5.06*	-1.62 ± 19.1	0.02	-20.4 ± 17.2	4.03 [‡]

Columns labeled “Effect” show the mean difference between children treated with the medication minus those not treated with it, adjusted for their scores at admission and for concurrently administered medications. Parentheses contain the 95% confidence interval for the adjusted mean difference.

Columns labeled “Test” indicate F values for continuous variables and likelihood ratio χ^2 for odds ratios.

* $P < 0.01$.

[†] $P < 0.05$.

[‡] $P < 0.10$.