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Effects of risperidone and parent training on adaptive functioning in children with pervasive developmental disorders and serious behavioral problems

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Abstract

Objective—Children with Pervasive Developmental Disorders (PDDs) have deficits in social interaction, delayed communication and repetitive behavior as well as impairments in adaptive functioning. Many children actually show decline in adaptive skills compared to age mates over time.

Method—This 24-week, three-site, controlled clinical trial randomized 124 children (4 through 13 years of age) with PDDs and serious behavior problems to medication alone (MED; N=49;

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The opinions and assertions contained in this report are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of Health and Human Services, the National Institutes of Health, or the National Institute of Mental Health. Drs. Dziura and Scahill had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. National Institute of Mental Health staff participated in the study design and implementation, analysis of the data, and composition of the manuscript.

This article is discussed in an editorial by Dr. Thomas W. Frazier on page xxx.

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risperidone 0.5 to 3.5 mg/day (if ineffective, switch to aripiprazole was permitted) or medication plus parent training (PT) (COMB; N=75). Parents of children in COMB received an average of 11.4 PT sessions. Standard scores and Age Equivalent scores on Vineland Adaptive Behavior Scales were the outcome measures of primary interest.

Results—Seventeen subjects did not have a post-randomization Vineland. Thus, we used a mixed model with outcome conditioned on the baseline Vineland scores. Both groups showed improvement over the 24-week trial on all Vineland domains. Compared to MED, Vineland Socialization and Adaptive Composite Standard scores showed greater improvement in the COMB group ($p = 0.01$ and 0.05 ; effect sizes = 0.35 and 0.22 , respectively). On Age Equivalent scores, Socialization and Communication domains showed greater improvement in COMB versus MED ($p = 0.03$, 0.05 ; effect sizes = 0.33 and 0.14 respectively). Using logistic regression, children in the COMB group were twice as likely to make at least 6 months gain (equal to the passage of time) in the Vineland Communication Age Equivalent score compared to MED ($p = 0.02$). After controlling for IQ, this difference was no longer significant.

Conclusion—Reduction of serious maladaptive behavior promotes improvement in adaptive behavior. Medication plus PT shows modest additional benefit over medication alone.

Keywords

risperidone; parent training; Pervasive Developmental Disorders; children; adaptive behavior

INTRODUCTION

Pervasive Developmental Disorders (PDDs) are chronic disorders of early childhood onset characterized by social deficits, communication delay, and repetitive behavior. The current prevalence estimate of 60-70 per 10,000 children is dramatically higher than previously accepted estimates.¹ This rise in prevalence is likely due to better community sampling methods, broader case definition and improved diagnostic precision.¹ Providing treatment for the growing number of children identified with PDDs is a major public health challenge. School districts confront increasing service demands and budget shortfalls.² In clinical settings, national insurance claims data from 2000-2004 reveal a 60% rise in the number of children diagnosed with PDDs and commensurate increases in cost.³

Children with PDDs may also show a range of behavioral problems including hyperactivity, impulsiveness, tantrums, aggression or self-injury in various combinations.^{4,5} These behavioral problems can undermine educational efforts and adversely influence everyday life for affected children and their families. To manage these behavioral problems, psychotropic medications are often part of the treatment plan.⁶ Parent surveys and administrative databases indicate rising use of atypical antipsychotics.^{7,8} Two medications in this class, risperidone and aripiprazole, are approved by the US Food and Drug Administration for the treatment of tantrums, aggression and self-injury in children with autistic disorder. Intensive behavioral intervention can also reduce these challenging behaviors,⁹ but these specialized services may not be available in all communities.

The Research Units on Pediatric Psychopharmacology (RUPP) Autism Network trial showed that risperidone was superior to placebo for reducing serious maladaptive behavior.¹⁰ Gains were stable over time, but symptom return was likely when the medication was withdrawn after six months of treatment.¹¹ Subsequently, we showed that the combination of medication and parent training was superior to medication alone in reducing serious maladaptive behavior in children with PDDs.¹² In this trial, we also measured change in adaptive behavior, which reflects the child's performance across socialization, communication and daily living domains. Children with intellectual disability

uncomplicated by PDD have adaptive skills that are consistent with their IQ scores. By contrast, children with PDDs have significantly lower levels of adaptive skills than their IQ scores would predict.¹³⁻¹⁵ We propose that serious behavioral problems contribute to the adaptive skill deficits in children with PDDs. Furthermore, reduction in these behavioral problems will lead to improvement in adaptive functioning. In this report, we test whether medication plus parent training (COMB) is superior to medication only (MED) on adaptive skills as measured by the Vineland Adaptive Behavior Scales.¹⁶

METHODS

Design

The study design has been described in detail in a previous publication.¹⁷ Briefly, 124 children were randomly assigned, in a 3:2 ratio, to MED (medication only, n=49) or COMB (medication plus parent training, n=75) for six months. The unbalanced randomization was intended to facilitate recruitment based on the assumption that families might prefer COMB treatment. The primary outcome measure was the parent-rated Home Situations Questionnaire on compliance in everyday life. Because a moderate or greater level of tantrums, aggression and self-injury was required for entry, the parent-rated Aberrant Behavior Checklist Irritability subscale was an essential secondary measure.¹² After the six-month randomized phase, subjects from both treatment groups who met *a priori* positive response criteria were invited to participate in a 10-week medication taper. The results of the discontinuation phase will be presented in a separate report.

Subjects and Setting

The RUPP Autism Network sites included: Indiana University, Ohio State University and Yale University. The study was approved by the institutional review board at each site. After obtaining informed consent, subjects were assessed for diagnosis, intellectual capacity, health status, behavioral problems and adaptive functioning.

Entry Criteria—Subjects were between 4 and 14 years with a DSM-IV-TR diagnosis of autistic disorder, Asperger's disorder or PDD—not otherwise specified (NOS) based on clinical assessment and corroborated by the Autism Diagnostic Interview—Revised (ADI—R).^{18,19} Subjects also had serious behavioral problems (e.g., tantrums, aggression and self-injury) as evidenced by a score of 18 or higher on the parent-rated Aberrant Behavior Checklist Irritability subscale (ABC-I)^{20,21} and a Clinical Global Impression - Severity score 4.²² Based on the Stanford-Binet 5, Leiter International Performance Scale, or the Mullen Scales of Early Learning, subjects had an IQ of 35 (or mental age of 18 months) or greater. Anticonvulsant treatment for seizures was permissible if the medication was stable (at least 4 weeks) and the subject was seizure-free (at least 6 months). Otherwise subjects were medication-free for two weeks for most psychotropic drugs (four weeks for fluoxetine). Children with a significant medical condition by history, examination or laboratory test, a lifetime diagnosis of psychosis, bipolar disorder, or current diagnosis of major depression, obsessive compulsive disorder, substance abuse, or girls with a positive Beta HCG pregnancy test were excluded. Screening for DSM-IV disorders was accomplished by the parent-completed Child and Adolescent Symptom Inventory.⁵ Randomization was conducted within site and stratified by Tanner stage (Tanner I or II versus Tanner III or higher), gender, diagnosis (autistic disorder versus other PDDs).

Measures for the Current Report

Home Situations Questionnaire—(HSQ)²³ is a parent-rated scale on compliance in everyday circumstances such as: “getting dressed,” “while you are on the telephone,” “when asked to do chores.” To ensure relevance for children with PDDs, we added five items to the

original 20-item HSQ: for example, “when asked to move from one activity to another,” “when repetitive behavior is interrupted.”²⁴ Questions answered affirmatively are rated on a 9-point Likert scale with higher scores indicating greater noncompliance. The resulting total of 1–9 ratings on “yes” items (range = 0–225) was divided by 25 to obtain a per item mean score.

Aberrant Behavior Checklist– Irritability (ABC-I) subscale.²⁰—The full ABC is a 58-item informant-based scale with five factor-analytically derived subscales: Irritability, Social Withdrawal, Stereotypy, Hyperactivity and Inappropriate Speech. The ABC-I is a 15-item measure of tantrums, aggression and self-injury. The correlation of the HSQ score and ABC-I score for the full sample of 124 study subjects at baseline was 0.30 ($P = 0.001$) suggesting that these ratings measure related, but separate, domains of behavior.

Vineland Adaptive Behavior Scales (Vineland).¹⁶—The Vineland is a parent interview designed to assess functional skills in three domains: Communication, Socialization, and Daily Living Skills. The Adaptive Composite Score estimates overall adaptive behavior. Vineland items are scored 0 (behavior not performed), 1 (performed sometimes) or 2 (performed on a regular basis). The instrument provides Standard scores (based on a population mean of 100 + 15) and Age Equivalent scores. To measure change, the Age Equivalent score provides an estimate of improvement (in months) against the passage of time.¹⁴

Noncompliance Index—To explore the impact of study treatments on compliance in everyday living situations, we derived the *Noncompliance Index* from the Vineland Daily Living Skills domain. The interview starts with simple examples to identify behaviors that the child performs on a regular basis (reflecting mastery). Subsequent items include incrementally more complex daily living skills, which are rated “performs sometimes” (scored 1) or “does not perform” (scored 0). The interview proceeds to identify items that are clearly beyond the child’s ability to perform (as evidenced by several items in a row scored “0”). Of interest for the Noncompliance Index were items scored 0 or 1 in the zone between mastery and clear inability. For each of these items, the primary caretaker was asked whether the child was unable to perform the behavior or unwilling to perform the behavior (due to noncompliance). The *Noncompliance Index* is the percentage of items that the child was unwilling to perform over the total number of items in this zone between mastery and clear inability. Higher scores indicate greater noncompliance. Because the number of items rated is different for each subject, coefficient alpha cannot be calculated. We calculated the percent agreement on the classification of inability or unwillingness to perform the behavior on 25 video-recorded interviews across five raters, who were blind to treatment. Of the total 553 relevant Daily Living Skill items, there were 509 agreements (92%) across the five raters. The Fleiss kappa coefficient, which adjusts for chance agreement, was 0.91.

Procedures

Once randomized, subjects were assessed weekly for 8 weeks, then every 4 weeks until Week 24. Two clinicians followed all subjects through the trial: an independent evaluator (who rated CGI scales and remained blind to treatment assignment throughout the trial) and a treating clinician. The treating clinician, who monitored adverse effects and adjusted the dose of the medication, was blind to treatment assignment for at least the first 8 weeks. To manage crises, consultation between the treating clinician and the behavioral therapist was permitted after Week 8.

Each assessment visit included a semi-structured review for adverse events, measurement of height, weight, vital signs and completion of several outcome measures. The Vineland and Noncompliance Index were administered at baseline and at Week 24 (or early termination) by the independent evaluator or another research team member who was blind to treatment assignment.

Given the six-month duration of the randomized trial and the planned Discontinuation phase, the trial had built-in nodal points (Weeks 8 and 24) to assess whether each subject's progress was sufficient to continue on study.^{12,17}

To minimize attrition, subjects who did not meet the positive response criterion at Week 8, (25% improvement on the parent-rated ABC-I and Much Improved or Very Much Improved on the CGI-I) could switch from risperidone to aripiprazole. Although both drugs are atypical antipsychotics, aripiprazole is presumed to have a different mechanism of action suggesting that it might be effective in cases when risperidone was not.^{17,25} During the 3-week switch to aripiprazole, subjects were seen weekly and parent training continued as scheduled for subjects in the COMB group. Twelve subjects switched to aripiprazole (6 in MED and 6 in COMB). In the current analysis, no distinction was made between subjects on risperidone or aripiprazole. Detailed analysis of outcomes for subjects who switched to aripiprazole will be presented in a separate report. Another procedure intended to minimize missing data during the trial included a planned early endpoint assessment for subjects who dropped out prematurely. These Vineland scores were carried forward to Week 24.

Adverse events were systematically assessed throughout the trial. The method of assessment as well as the frequency and types of adverse events were described in a previous report.¹²

Treatments

Parent Training—The structured parent training (PT) program included 11 core sessions, one home visit, and up to 3 optional sessions during the first 16 weeks of the trial. Booster sessions between Weeks 16 and 24 (two by telephone, one in clinic and a home visit) were provided for review and support.²⁶ The 75- to 90-minute therapy sessions were delivered individually to the primary caregiver (a spouse or significant other could also attend) by doctoral- or master's-level clinicians. Early sessions identified the antecedent, purpose and reinforcements of the maladaptive behaviors. For example, in response to a child's extreme protest and refusal to get dressed, some parents may, understandably, complete this task for the child. This pattern limits the acquisition and regular performance of everyday living skills. Subsequent sessions taught parents to manage antecedents of maladaptive behavior, enhance structure with daily schedules and use selective ignoring to avoid reinforcing negative behavior. These strategies were followed by sessions focused on promoting compliance, functional communication, daily living skills and generalization of skills across time and place. Sessions employed direct instruction, video vignettes for illustration, role-playing and review of individually assigned homework between sessions.²⁶

Therapists were certified after demonstrating at least 80% fidelity to the PT manual with a training case. Thereafter, all PT sessions were recorded on video and review of a 10% random sample of recorded sessions demonstrated fidelity to the manual.¹²

Dosing of Risperidone and Aripiprazole: The weight-based dosing schedule has been described in detail in previous publications.^{12,17} For example, youngsters weighing > 20 and 45 kg were started on risperidone 0.5 mg/day and increased gradually to a maximum of 2.5 mg/day over 29 days. The treating clinician was allowed to decrease the medication or delay a scheduled increase to manage adverse effects. For subjects who switched to

aripiprazole, it was initiated at 2.5 mg per day and gradually increased while risperidone was simultaneously tapered over a 3-week period.

Data Analyses

Baseline characteristics were compared between treatment groups with t-tests for continuous variables and chi-square for categorical variables. We used a hierarchical approach to analysis and set the alpha at 0.05 for evaluating the first primary outcome measure (HSQ). Because change on the HSQ was significantly different across the two groups, Vineland analyses proceeded without correction.^{12,17} The significance value for the Noncompliance Index was reset to 0.025 (0.05 divided by 2).

The original analytic plan for mean Vineland Standard and Age Equivalent scores included least squares means from an ANCOVA model adjusted for site, IQ and Vineland baseline scores. Due to attrition (17 of 124 subjects with no post-randomization Vineland assessment), we conducted a mixed model that used all available data including both baseline and all post-randomization Vineland scores to estimate treatment effects. This conditional joint response model is more tolerant of missing data than our originally planned ANCOVA model and less biased than carrying baseline data forward to endpoint. The mixed model assumes that missing data are missing at random and provides unbiased estimates of treatment effects provided that missing data are independent of response given observable data. Treatment differences were estimated conditional on baseline response.²⁷

Using only the 107 subjects with post-randomization Vineland scores, we conducted exploratory logistic regression models to compare the unadjusted rate of subjects in each treatment group who gained at least 6 months on Vineland Age Equivalent scores (equal to the passage of time). Logistic regression models then adjusted for selected baseline characteristics (IQ greater than or equal to 70 versus below 70) to determine whether these categorical metrics affected the association between treatment group and achievement of at least six months gain on Vineland Age Equivalent score. To check for effect modification, we also evaluated interaction between treatment and IQ (greater than or equal to 70 versus below 70). Additional exploratory analyses calculated the correlation of change scores on the Vineland standard scores and the measures of maladaptive behavior (the ABC-I and the HSQ). Exploratory analyses are presented without correction for multiple comparisons.

RESULTS

One hundred ninety nine subjects were screened across the three recruitment sites.¹² Of these, 124 subjects (105 boys and 19 girls) were randomly assigned to COMB (n=75) or MED (n=49). As per protocol, five subjects were withdrawn from the trial at Week 8 due to lack of efficacy (these subjects had previous unsuccessful trials of aripiprazole). Over the course of the 24-week trial, an additional 24 subjects exited early (9 between baseline and Week 8; 6 between Weeks 12 and 15; 9 between Weeks 16 and 23). There was no difference in the rate of attrition by treatment ($\chi^2 = 0.02$; $p = 0.88$). Of the 29 subjects who exited early, 12 subjects returned for post-randomization Vineland; the mean number of weeks for the repeat Vineland was 23.05 ± 3.30 (range 7 to 27). Thus, 17 subjects did not return for post randomization Vineland assessment. These 17 subjects had lower scores on the ABC-Inappropriate Speech subscale and were more likely to be rated *moderate* on the CGI-Severity at baseline compared the 107 subjects with a repeat Vineland. Based on other ABC subscales, HSQ, Vineland scores and rate of intellectual disability, however, there were no other indications that subjects without a repeat Vineland score were less severe (data not shown). The mixed model included all 124 subjects in the primary analysis of Vineland mean scores.

Table 1 shows the demographic and clinical characteristics by treatment assignment. The ABC-Stereotypy subscale was higher in the MED group (see Table 1). Because we used different intelligence tests across the range IQ in this sample, IQ is reported as a categorical variable (greater than or equal to 70 and below 70). The 46% of children with intellectual disability in the MED group (23 of 49) was slightly higher than the 37% in the COMB group (27 of 73 [missing data on two subjects]) ($\chi^2 = 3.08$; $p = .08$). Across all Vineland domains, mean baseline values were significantly lower in the MED group, which is consistent with the greater proportion of subjects with IQ below 70 in MED group (Vineland scores in Table 2).

At endpoint, the average dose of risperidone was higher (2.26 mg/day; 0.071 mg/kg) than in the COMB group (1.98 mg/day; 0.066 mg/kg) ($p = .04$, two-sided test). The families in COMB treatment received an average of 11.4 ± 2.62 PT sessions. [Note: the mean number of sessions attended is based on the sample of 107 subjects with post-randomization Vineland and differs slightly from our previous report.¹²] The average Vineland Standard and Age Equivalent scores indicate that this sample was functioning far below chronological age at baseline. At endpoint, Standard scores, Age Equivalent scores and the Noncompliance Index all showed meaningful gains in both groups (Table 2). Compared to MED, the Socialization and Adaptive Composite Standard scores showed greater improvement in the COMB group ($p = 0.01$ and 0.05 ; effect sizes = 0.35 and 0.22 , respectively). On Age Equivalent scores, Socialization and Communication domains showed greater improvement in COMB versus MED ($p = 0.03$, 0.05 ; effect sizes = 0.33 and 0.14 respectively). Table 2 also shows a significant decline in the Noncompliance Index in the COMB treatment group compared to MED ($p = .03$; effect size = 0.30).

Table 3 provides the proportion of subjects in each group who achieved six months or greater gain on Vineland Age Equivalent domains by treatment group. The percentage of subjects in the COMB group who achieved at least six months gain was greater than MED on all Vineland domains. The logistic regression model showed a significant odds ratio for six months gain in the Communication domain for COMB versus MED (odds ratio = 2.64 ; 95% CI = 1.18 , 5.93 ; $p = 0.02$). When adjusted for IQ, the group difference in the Communication domain was no longer significant (odds ratio = 2.21 , 95% CI = 0.93 , 5.26 , $p = 0.07$).

Further examination of IQ and treatment response showed that IQ (≥ 70 versus < 70) did not affect the odds ratio Daily Living Skills. On the Socialization domain, the main effect of treatment remained non significant, but subjects with IQ of 70 or greater had a 3-fold greater likelihood of achieving 6 months gain than subjects with IQ less than 70 (odds ratio = 2.97 , 95% CI = 1.29 , 6.87 , $p = 0.01$). However, there was no treatment by IQ interaction suggesting that observed gains in subjects in the normal IQ range was not different by treatment group. Subjects in the average IQ range were more likely to show at least 6 months gain on the Vineland Communication domain (odds ratio of 4.89 , 95% CI 2.07 , 11.53 , $p = 0.0003$). Once again, there was no treatment by IQ interaction.

With the exception of the Vineland Communication score and the ABC-I subscale, correlations between the change in the Vineland standard scores and the change in the HSQ and ABC-I were significant in the sample as a whole (Table 4). When examined by treatment group, there was no clear pattern suggestive of a stronger association between Vineland scores and maladaptive scores as measured on the ABC-I and HSQ (data not shown).

DISCUSSION

The study model predicted that, compared to medication alone, medication plus PT would promote greater reduction in noncompliant and disruptive behavior leading to improved adaptive functioning over time. Thus, the proximal outcomes (maladaptive behavior that brought the subjects into the study) were conceptually linked to more distal outcomes (adaptive functioning). In a previous report we showed that COMB was superior to MED in reducing maladaptive behavior.¹² This report evaluated the impact of combined treatment on adaptive behavior over six months of treatment.

The MED and COMB groups both showed improvement on Vineland Standard and Age Equivalent scores across all domains. This observation is counter to the expected loss of adaptive skill in children with PDDs over time.^{13,15} Adjusted for IQ, mean Vineland Standard scores for Socialization domain and Adaptive Composite were significantly greater for COMB versus MED. On the mean Age Equivalent scores (also adjusted for IQ), the Socialization and Communication domains showed greater improvement in COMB versus MED. The Socialization domain includes items on social motivation (“Shows interest in activities of others”) and items that are relevant to PT (“Follows time limits set by caregiver”) and medication (“controls anger or hurt feelings when denied own way”). In addition to basic skills, the Communication domain also contains items that reflect compliance (“Follows instructions requiring an action and an object”) and functional communication (“Delivers a simple message”).

Contrary to our prediction, improvement in the Vineland Daily Living Skills domain was not significantly greater in the COMB group. This appears to be due to notable gain in the MED group, which is consistent with results from our previous trial.¹⁴ On the Noncompliance Index, (derived from the Daily Living domain), the COMB group showed a significant improvement compared to MED. This finding suggests that COMB treatment mitigated the role of defiance (refusal versus inability) on the performance of daily living skills.

The percentage of subjects in COMB treatment who achieved six months or greater gain on Vineland Age Equivalent scores was larger than the MED group across all domains, but only significant for the Communication domain. Subjects in COMB treatment were twice as likely to achieve this benchmark in the Vineland Communication as the MED group. When adjusted for IQ, however, this finding was no longer significant.

Exploratory logistic regression analysis on the benchmark of six months gain (equal to the passage of time) in Vineland Age Equivalent scores showed greater gains in both treatment groups in Socialization and Communication domains in children within the normal IQ range versus those below 70. However, there was no evidence of interaction between IQ and treatment group. The failure to detect such an interaction may be due to the limited sample size. To date, there have been few randomized trials of PT in children with PDDs (reviewed in ^{26,28,29}). In addition, the term *parent training* in children with PDDs is used to describe a range of interventions focused on language, joint attention, social skill development and disruptive behavior. A retrospective analysis of 32 adolescents with PDDs from a specialized treatment center provided preliminary evidence that child-based, intensive behavioral intervention and antipsychotic medication was more effective than behavioral intervention alone in reducing aggression.³⁰ To our knowledge, however, no previous trial has evaluated the combined effects of medication and a structured PT program focused on reducing disruptive behavior and improving adaptive behavior versus medication alone. Thus, it is difficult to compare our results with prior studies.

Dawson et al. (2009) conducted a two-year randomized trial in 48 children with PDDs (age 18 months to 2.5 years).³¹ One group received 20 hours per week of child-focused intervention with some parent training; the other group received treatment as usual (average 9 hours per week of individual treatment in various special education settings). At baseline, Vineland Standard scores ranged from 69 to 87 across domains. With the exception of Communication, Vineland Standard scores declined from baseline in both groups after one year of treatment. After two years, the Communication score continued to improve in the intensive treatment group compared to no change in the control group. Standard scores on the Socialization, Adaptive Composite and Daily Living Skills actually went down in both groups. The statistically significant difference on the Adaptive Composite and Daily Living Skills scales for the intensive treatment group was due to greater declines in the control group. A similar pattern of greater decline in the control group was reported by Smith et al.³²

In the current study, both treatment groups showed improvement on all Vineland domains. First, baseline Vineland scores in our sample were lower than these prior studies suggesting that severe maladaptive behavior interferes with acquisition and regular performance of adaptive skills resulting in the lower scores at baseline. Second, the reduction in noncompliant and disruptive behavior by medication or combined treatment promoted gains in adaptive functioning for both groups.

Although this is among the largest randomized clinical trials in children with PDDs to date, the power to detect small differences between two active treatments was limited. Indeed, both groups improved on virtually all measures suggesting that the finding of no statistical difference between groups on some measures may be related to sample size. It may be argued that there should have been a PT only group (to measure the effect of parent training alone) or medication plus a less specific parent education program (to control for attention). However, the addition of a third treatment group would have substantially increased the duration and cost of the study. For example, a three-group study designed to detect a difference between two combined treatments (drug plus PT versus drug plus parent education), would have required a 50% increase in the sample size and would likely have taken another two years to complete. Finally, risperidone produced rapid and enduring reduction of serious behavioral problems in most children in this sample as in our previous study.^{10-12,14} Inclusion of a PT only group would not have been a fair comparison and would not meet the equipoise standard.

The findings of this analysis extend the results of our previous report that showed additive benefits of PT to medication in school-age children with PDDs and serious behavioral problems. In general, adaptive skills are not expected to keep pace with time in children with PDDs. The added effects of PT on adaptive functioning over and above the benefits of risperidone alone were modest and not evident on all adaptive outcomes measured. Nevertheless, the observed benefits in adaptive functioning in both treatment groups over the six-month trial suggest that reducing serious behavioral problems can enhance the quality of life in this vulnerable population.

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Table 1

Baseline Demographic and Clinical Features of Medication Alone (MED) and Medication Plus Parent Training (COMB) Groups (N=124)

Variable	MED (49)	COMB (75)	p-Value
Mean Age Year (SD)	7.50 (2.80)	7.38 (2.21)	.86
	N (%)	N (%)	
PDD Diagnosis			
Autistic Disorder	32 (65.3)	49 (65.3)	.83
PDD-NOS	13 (26.5)	22 (29.3)	
Asperger's Disorder	4 (8.2)	4 (5.3)	
IQ Category ^a			
> 70	23 (46.9)	46 (63.0)	.08
< 70	26 (53.1)	27 (37.0)	
Anticonvulsant Medication	4 (8.2)	0 (0.0)	.02
Clinical Global Impression - Severity			
Moderate (4)	14 (28.6)	25 (33.3)	.47
Marked (5)	19 (38.8)	33 (44.0)	
Severe (6)	15 (30.6)	17 (22.7)	
Extreme (7)	1 (2.0)	0 (0.0)	
Race and Ethnicity ^b			
White/Non-Hispanic	34 (69.4)	59 (78.7)	.15
Hispanic	7 (14.3)	4 (5.30)	
African American	7 (14.3)	9 (12.1)	
Asian American	0 (0.0)	3 (4.0)	
Native American	1 (2.0)	0 (0.0)	
Educational Placement			
F/T, Regular Education	10 (20.4)	18 (24.0)	.44
F/T, Regular Education, with Aide	0 (0.0)	3 (4.0)	
Regular Ed, with Some Special Ed.	5 (10.2)	4 (5.3)	
Special Education Classroom	8 (10.3)	14 (18.7)	
Special Elementary School	3 (6.1)	2 (2.7)	
Home School	4 (8.2)	5 (6.7)	
Special Preschool	11 (22.4)	11 (14.7)	
Regular Preschool	6 (12.2)	8 (10.7)	
No School	2 (4.1)	12 (16.0)	
	Mean (SD)	Mean (SD)	
HSQ			
Average Severity Score	4.16 (1.47)	4.31 (1.67)	.61
"Yes" Count	18.9 (3.46)	18.6 (4.65)	.73
ABC			
Irritability	29.7 (6.10)	29.3 (6.97)	.77
Social Withdrawal	17.1 (8.37)	15.2 (9.01)	.22

Variable	MED (49)	COMB (75)	p-Value
Stereotypic Behavior	10.6 (5.46)	7.59 (5.20)	.003
Hyperactivity/Noncompliance	36.1 (6.86)	35.3 (9.30)	.61
Inappropriate Speech	6.37 (4.03)	5.75 (3.43)	.36

Note. ABC= Aberrant Behavior Checklist; F/T = full time; HSQ = Home Situations Questionnaire; NOS = not otherwise specified; PDD = pervasive developmental disorder.

^a2 subjects in COMB group had missing data on IQ;

^bParticipants classified themselves for ethnicity

Table 2

Vineland Standard and Age Equivalent scores using all observed data with response conditioned on Baseline (N=124)

	MED (N=49)		COMB (N=75)		Adjusted Mean Difference ^b (SE)	95% CI for Adjusted Mean Difference (Lower, Upper)	P value ^c (effect size ^d)
	Baseline	Week 24	Baseline	Week 24			
Vinland Score ^a							
Standard Score							
Daily Living Skills	41.14 (19.81)	45.34(20.48)	50.79 (18.49)	55.65 (21.86)	2.44(2.47)	(−2.46,7.34)	0.33 (0.13)
Socialization	53.48 (14.41)	56.59 (17.38)	59.55 (15.01)	67.42 (18.48)	5.16(1.96)	(1.27,9.06)	0.01(0.35)
Communication	53.18(19.94)	53.57 (20.23)	61.15 (20.95)	63.90 (22.65)	3.03(1.76)	(−0.46,6.52)	0.09 (0.15)
Adaptive Composite	45.84 (15.50)	47.84 (15.81)	53.15(15.66)	57.87(19.03)	3.46(1.78)	(−0.06,6.99)	0.05 (0.22)
Age Equivalent Score							
Daily Living Skills	2.85(1.52)	3.49 (1.72)	3.63 (1.94)	4.36 (2.25)	0.12(1.92)	(−0.26,0.50)	0.55 (0.06)
Socialization	2.09 (1.08)	2.71 (1.51)	2.80 (1.84)	3.99 (2.56)	0.51(0.24)	(0.05,0.98)	0.03 (0.33)
Communication	3.12 (2.15)	3.42 (2.18)	3.99 (2.65)	4.58 (2.85)	0.34(0.17)	(0.01,0.68)	0.05 (0.14)
Noncompliance Index	18.91(14.18)	12.88 (10.83)	16.59 (11.44)	8.41 (8.69)	−3.76(1.71)	(−7.15,−0.38)	0.03 (0.30)

Note: CI = confidence interval; COMB = medication plus parent training; MED = medication alone; SE = standard error.

^a Data are presented as Least Squares Mean (SD) from the mixed model.

^b Adjusted Mean Difference = difference of Least Squares Means from Mixed model conditioned on Baseline score, IQ, Clinical Global Impression (CGI)-Severity and Aberrant Behavior Checklist (ABC) Inappropriate Speech subscale.

^c P-value from Mixed model conditioned on Baseline score, IQ, CGI-Severity and ABC Inappropriate Speech subscale. Bold indicates p-value less than 0.05.

^d Effect size calculated from adjusted mean difference divided by pooled standard deviation at baseline.

Table 3

Proportion and probability of subjects gaining at least 6 months on Vineland Age Equivalent scores by treatment group (N=107)

Vineland Domain	MED (N=42)		COMB (N=65)		OR	95% CI for OR (Lower, Upper)	P value
	< 6 months N (%)	6 months N (%)	< 6 months N (%)	6 months N (%)			
Daily Living Skills	19 (45.2)	23 (54.8)	27 (41.5)	38 (58.5)	1.16	0.53, 2.54	0.71
Socialization	17 (40.5)	25 (59.5)	21 (32.3)	44 (67.7)	1.43	0.64, 3.19	0.39
Communication	28 (66.7)	14 (33.3)	28 (43.1)	37 (56.9)	2.64	1.18, 5.93	0.02

Note: CI = confidence interval; OR= odds ratio.

Note: Table only includes subjects with a post-randomization Vineland assessment. Bold indicates p-value less than 0.05.

Range: Daily Living Skills (Medication Plus Parent Training (COMB)=1 to 60 months; Medication Alone (MED) 1 to 32 months); Socialization (COMB= 1 to 55 months; MED=1 to 38 months); Communication (COMB= 1 to 38 months; MED = 1 to 34 months)

Table 4

Pearson correlation coefficients for change in Vineland Standard scores and change in Home Situations Questionnaire (HSQ) and Aberrant Behavior Checklist –Irritability (ABC-I) scores for 107 subjects with a post baseline Vineland interview

	Change in HSQ	p-value	Change in ABC-I	p-value
Daily Living Skills	–0.24	0.01	–0.22	0.02
Socialization	–0.22	0.02	–0.30	0.001
Communication	–0.25	0.01	–0.14	0.16
Adaptive Behavior Composite	–0.22	0.02	–0.21	0.03

Note: Correlations are negative because improvement in Vineland scores go up whereas improvement on the HSQ and ABC-I scores go down