

Risperidone and Adaptive Behavior in Children With Autism

SUSAN K. WILLIAMS, PH.D., LAWRENCE SCAHILL, M.S.N., PH.D.,
BENEDETTO VITIELLO, M.D., MICHAEL G. AMAN, PH.D., L. EUGENE ARNOLD, M.ED., M.D.,
CHRISTOPHER J. McDOUGLE, M.D., JAMES T. McCracken, M.D., ELAINE TIERNEY, M.D.,
LOUISE RITZ, M.B.A., DAVID J. POSEY, M.D., NAOMI B. SWIEZY, PH.D., JILL HOLLWAY, M.A.,
PEGEEN CRONIN, PH.D., JASWINDER GHUMAN, M.D., COURTNEY WHEELER, B.S.,
DOMENIC CICHETTI, PH.D., AND SARA SPARROW, PH.D.

ABSTRACT

Objective: To evaluate the impact of risperidone on adaptive behavior in children with autistic disorder who have serious behavior problems and to examine different methods of scoring the Vineland Adaptive Behavior Scales to measure change. **Method:** Forty-eight children (5 years to 16 years, 5 months) who showed behavioral improvement during acute treatment with risperidone were followed for 6 months and assessed with the Vineland Scales. **Results:** Raw scores, age-equivalents, and special norm percentile scores all showed significant increases in adaptive behavior in the areas of communication, daily living skills, and socialization ($p < .01$). During a period of 6 to 8 months, children gained an average of 7.8 age-equivalent months in the area of socialization, a >6% improvement beyond what would be expected based on baseline growth rates. **Conclusions:** Although limited by the absence of a control group, these results suggest that risperidone may improve adaptive skills in children with autistic disorder accompanied by serious behavioral problems. Vineland age-equivalent scores appear to be most useful in assessing change with treatment over time. *J. Am. Acad. Child Adolesc. Psychiatry*, 2006;45(4):431–439. **Key Words:** autism, risperidone, Vineland Adaptive Behavior Scales.

Autistic disorder (autism) is a chronic developmental disorder of early onset characterized by deficits in social interaction and communication, along with repetitive behavior and restricted interests. In addition to these core features, children with autism often exhibit aggression, self-injury, or tantrums and nearly always have deficits in adaptive behavior, which negatively affect quality of life.

Several investigators have cited the need for the identification of reliable and socially valid outcome measures that are sensitive to change in treatment studies with this population (Scahill and Lord, 2004; Wolery and Garfinkle, 2002). Measures should not only assess whether a child has learned a specific skill or improved on a specific set of target symptoms but also assess the degree to which the child uses and adapts new skills in

Accepted October 11, 2005.

The opinions and assertions contained in this report are the private views of the authors and are not to be construed as reflecting the views of the Department of Health and Human Services, the National Institutes of Health, or the National Institute of Mental Health. These data were in part presented as a poster at the Annual Meeting of the Association for the Advancement of Behavior Therapy, New Orleans, November 2004.

This study was part of the research activities of the Research Units on Pediatric Psychopharmacology (RUPP) Autism Network: Drs. McCracken and Cronin at the University of California, Los Angeles; Drs. Aman and Arnold and Ms. Hollway at Ohio State University, Columbus; Drs. McDougle, Posey, and Swiezy at Indiana University, Indianapolis; Drs. Scahill, Williams, Cichetti, and Sparrow at Yale University, New Haven, CT; Drs. Tierney and Ghuman

and Ms. Wheeler at Kennedy Krieger Institute, Baltimore, MD; and Dr. Vitiello and Ms. Ritz at the National Institute of Mental Health, Bethesda, MD. The RUPP network was funded by National Institute of Mental Health grants N01MH70001 to Indiana University, N01MH80011 to Ohio State University, N01MH70010 to UCLA, N0MH70009 to Yale University. The authors thank Allison Lancor and Arlene Kohn for study coordination; James Robinson, M.E.D., and Shirley Chuang, Ph.D., for data management; and Helen Tager-Flusberg, Ph.D., for advice on the interpretation of results.

Correspondence to Dr. Lawrence Scahill, Yale Child Study Center, P.O. Box 207900, New Haven, CT 06520-7900; e-mail: lawrence.scahill@yale.edu.

0890-8567/06/4504-0431©2006 by the American Academy of Child and Adolescent Psychiatry.

DOI: 10.1097/01.chi.0000196423.80717.32

natural environments (e.g., at home). Assessment of adaptive functioning is considered important because adaptive skill is closely related to functional independence and quality of life (Scahill and Lord, 2004). The Vineland Adaptive Behavior Scales (Sparrow et al., 1984) are frequently used to measure adaptive behavior. The Vineland assesses a person's actual behaviors (as opposed to ability to perform a behavior) across three domains: communication, daily living, and socialization. By not requiring the child's participation, through a clinical interview with the parent, the Vineland produces a valid assessment of the child's day-to-day functioning that cannot often be readily assessed by either direct observation or administration of tasks (Sparrow et al., 1984).

Several studies using the Vineland (Bolte and Poustka, 2002; Freeman et al., 1988; Gillham et al., 2000; Kraijer, 2000; Stone et al., 1999; Volkmar et al., 1993) have documented a characteristic profile of adaptive skills in children with autism: a relative deficit in socialization, strength in daily living skills, and communication scores falling between these two extremes. In addition, global adaptive behavior in children with autism is significantly below intellectual ability, and, although they can make gains in adaptive skills, they rarely catch up to their mental age peers. Children with autism also demonstrate greater variability on Vineland items when compared with children with mental retardation only (Burack and Volkmar, 1992; VanMeter et al., 1997).

Although the Vineland has not been commonly used as an outcome measure, this use has been suggested (Carter et al., 1998). Studies that have used it as an outcome measure, however, have not used consistent scoring methods. Some investigators examined standard scores (Bolte and Pustka, 2002; Eikeseth et al., 2002; Panerai et al., 2002; Smith et al., 2000a, b). Others used special norm standard scores (Bibby et al., 2002) or age-equivalents (Harris et al., 1995). These differences make it difficult to draw general conclusions.

A failure to observe meaningful treatment gains in adaptive behavior in some studies (e.g., Smith et al., 2000a, b) may be caused by small sample sizes, non-specific interventions for adaptive skills, or the choice and scoring of the Vineland as an outcome measure. Studies using standard scores have reported that children with autism decline in adaptive behavior with age (Carter et al., 1998; Fisch et al., 2002). By contrast, studies using age-equivalents demonstrate that they can make gains in

adaptive skills but at a slower rate than typical peers (Charman et al., 2004; Schatz and Hamdan-Allen, 1995). Standard scores based on national norms or on autism-specific norms may be most easily interpretable for baseline characterization. Because the standardization process reduces variability (floor effects for low-functioning individuals), however, they may not be sensitive enough for measuring change over short time periods. Given the limitations of Vineland standard scores for measuring change, alternative scoring methods may be useful (Carter et al., 1998).

Adaptive skill is an area of critical deficit for children with autism. Failure to acquire new adaptive skills with age often translates into greater functional disability. The purpose of the present study was to evaluate the change in adaptive functioning in a group of children with autism who were treated with risperidone for 6 months. Risperidone is an atypical antipsychotic that has been shown to be effective in decreasing serious behavior problems in children with autism (Research Units on Pediatric Psychopharmacology [RUPP] Autism Network, 2002, 2005). A second important aim was to evaluate which method of scoring the Vineland is most sensitive to change.

METHOD

Participants and Procedures

To address these aims, data from a group of children who were successfully treated with risperidone in the RUPP study, a multisite randomized clinical trial (RUPP Autism Network, 2002), were evaluated. That study found that risperidone was effective in reducing disruptive behavior in children diagnosed with autism accompanied by aggression, tantrums, and self-injury (RUPP Autism Network, 2002, 2005). The full sample consisted of 101 children (82 males) diagnosed with autism, ranging in age from 5 to 17 years (mean 8.9 ± 2.11 years). Table 1 displays baseline descriptive data for the full sample, the 63 subjects who showed a positive response to risperidone and the subgroup of 48 who had usable data for analyses. At baseline, all subjects were medication-free except two who were taking stable doses of anticonvulsants for seizures. Written informed consent was provided by the parent or guardian.

The study design has been described in detail elsewhere (Scahill et al., 2001). Briefly, there were three phases: an acute 8-week double-blind, placebo-controlled phase (RUPP Autism Network, 2002), a 4-month open-label extension for children who responded positively to risperidone, and a placebo-controlled discontinuation (RUPP Autism Network, 2005). Children initially randomized to placebo in the acute phase who failed to show significant improvement were treated in a supplemental 8-week open-label trial with risperidone. The placebo nonresponders who showed a positive response to risperidone in this open trial were also invited to participate in the 4-month additional phase of open-label treatment.

Positive response in the acute phase was defined by 25% reduction in the parent-rated Aberrant Behavior Checklist (ABC)

TABLE 1
Demographics and Functioning Characteristics of
Study Sample at Baseline

	Percentage		
	Original (<i>n</i> = 101)	Responders (<i>n</i> = 63)	Final (<i>n</i> = 48)
Male	81	78	83
Ethnicity			
White	66	68	71
African American	11	9	2
Asian/Pacific Islander	8	8	8
Hispanic/Latino	7	5	6
Other	8	10	13
Cognitive ability (IQ)			
No score	10	10	10
Average (≥ 86)	5	5	4
Borderline (71–85)	12	11	15
Mild MR (50–70)	25	27	23
Moderate MR (36–49)	18	19	19
Severe MR (21–35)	16	17	21
Profound MR (≤ 20)	15	11	8
Variable	Mean \pm SD		
Age, yr	8.9 \pm 2.11	8.5 \pm 2.30	8.3 \pm 2.10
ADI-R Recip. Social Inter.	26.05 \pm 3.87	25.86 \pm 4.03	26.21 \pm 3.41
Aberrant Behavior Checklist			
Irritability	25.82 \pm 7.53	26.79 \pm 7.59	27.13 \pm 7.20
Social withdrawal	16.35 \pm 8.56	15.86 \pm 8.13	15.58 \pm 7.57
Stereotypy	9.88 \pm 4.83	10.38 \pm 4.57	10.29 \pm 4.39
Hyperactivity	31.95 \pm 9.31	33.51 \pm 8.86	34.35 \pm 8.02
Inappropriate speech	5.89 \pm 4.51	6.27 \pm 4.89	5.96 \pm 4.21
Vineland [standard scores (age-equivalents in months)]			
Communication	43.27 \pm 15.51 (34 \pm 24)	43.33 \pm 14.13 (32 \pm 23)	43.58 \pm 13.48 (31 \pm 23)
Daily living skills	35.50 \pm 16.73 (38 \pm 17)	37.60 \pm 17.31 (37 \pm 17)	39.42 \pm 18.06 (38 \pm 17)
Socialization	48.33 \pm 13.01 (25 \pm 18)	47.38 \pm 10.26 (22 \pm 13)	48.67 \pm 9.78 (22 \pm 13)
Composite	45.15 \pm 14.72 (33 \pm 17)	41.05 \pm 14.97 (31 \pm 16)	42.35 \pm 15.79 (31 \pm 16)

Note: MR = mental retardation; ADI-R Recip. Social Inter. = Autism Diagnostic Inventory-Revised Reciprocal Social Interaction.

Irritability subscale score plus a clinician-rated Clinical Global Impressions-Improvement score of “much improved” or “very much improved.” The clinician was blind to treatment condition. Sixty-three children (33 from double-blind, 30 from the open-label trial for placebo nonresponders) showed a positive response and were followed for an additional 4 months to examine the impact of 6 months of medication.

Measures

Before randomization into the acute phase and again at 6 months, participants received an extensive battery of measures, including the ABC (Aman et al., 1985a) and the Vineland (Sparrow et al., 1984). The diagnosis of autism was based on clinical evaluation and corroborated by the Autism Diagnostic Inventory-Revised (ADI-R; Lord et al., 1994).

ABC. The ABC is a 58-item informant-based scale composed of five subscales. The five scales are labeled as follows: Irritability (agitation, crying, and self-injurious behaviors; 15 items); Lethargy/Social Withdrawal (16 items); Stereotypic Behaviors (rituals, meaningless body movements; seven items); Hyperactivity (16 items); and Inappropriate Speech (excessive talking, repeating phrases; four items). The ABC was developed as a measure of severity and treatment effects for patients with developmental disabilities. Multiple studies confirm the reliability and validity of the factor structure, distribution of scores, and sensitivity to change (Aman et al., 1985b; Brown et al., 2002; Marshburn and Aman, 1992).

ADI-R. The ADI-R is a highly structured parent interview used to support a clinical impression of autism in children and adults. It has demonstrated excellent reliability and validity for the diagnosis of autism. The training for the ADI-R involves a set of didactic sessions, supervised administration by an expert interviewer, and demonstrated reliability on the part of the ADI-R trainee.

Vineland Adaptive Behavior Scale. The Vineland is a parent interview designed to measure the child's functional competence in activities of daily living. It has been normed using national samples and is used extensively in studies of children with developmental disabilities and has excellent reliability and validity. The interview, which is conducted in a semistructured manner, establishes the child's actual performance of skills across three domains: communication, socialization, and daily living skills. In each domain, the interviewer begins with broad queries about the child's adaptive behavior. Additional questions are asked to identify skills that the child has acquired and performs on a regular basis (score of 2), skills that are performed sometimes (score of 1), or not at all (score of 0). Items are specific and arranged in increasing complexity. In general, however, the interviewer does not read the items from the page and asks the parent to respond directly. For example, rather than ask directly if the child can recite the alphabet, the interviewer engages in a discussion of letter recognition, word recognition, reading, and so forth. This semistructured approach permits the scoring of several clustered items. Finally, the scores on the first three domains are used to derive an adaptive behavior composite score, which is a global estimate of adaptive behavior.

Intellectual Functioning. Children were administered one of several tests of cognitive ability: WISC-III (Wechsler, 1991; 26% of sample), Leiter International Performance Scale-Revised (Roid and Miller, 1997; 32%), Mullen Scales of Early Learning (Mullen, 1995; 39%), or Wechsler Preschool and Primary Scale of Intelligence-Revised (Wechsler, 1989; 3%). Because several different tests were used, children were classified categorically (average ability, borderline intellectual functioning, and mild, moderate, or severe mental retardation).

Statistical Analyses

The goals of this study were to determine whether effective treatment with risperidone had a positive effect on children's adaptive behavior (above expected change resulting from the passage of time alone) and to evaluate the sensitivity of the Vineland in

detecting such an effect. First, we compared the baseline characteristics of the full sample ($n = 101$) to the 63 children who showed a positive response to treatment (i.e., $\geq 25\%$ reduction on the Irritability subscale and much or very much improved on the Clinical Global Impressions–Improvement). The purpose of this analysis was to determine whether the subjects who entered the 4-month extension phase were different from those who did not.

At follow-up, 48 of the 63 children who showed a positive response had full data across all Vineland scores for both baseline and week 24 of treatment. Of the 15 subjects without Vineland interviews, 3 were missing and 12 exited the study early. At baseline, these 15 subjects were not significantly different from the 48 with full data. The Vineland scores at baseline and follow-up for the 48 subjects are shown in Table 2. The baseline standard scores for the 15 without endpoint data were communication, 42.53 ± 16.53 ; daily living skills, 31.80 ± 13.55 ; and socialization, 43.27 ± 11.04 . At follow-up assessment, all 48 subjects had been treated with risperidone for 24 weeks; however, the length of time between baseline and follow-up assessments varied. Subjects initially randomized to risperidone who showed a positive response ($n = 26$) were reevaluated after 24 weeks. By protocol design, those initially assigned to placebo ($n = 22$) who did not improve were then treated in an 8-week open-label trial and had follow-up assessment approximately 32 weeks after baseline.

To examine the impact of risperidone treatment on adaptive functioning, the change in the Vineland scales from baseline to 6-month follow-up was computed. Four indices were used to examine change in adaptive skills: (1) raw scores, (2) standard scores based on national norms, (3) percentile rank scores based on derived

autism norms (Carter et al., 1998), and (4) age-equivalent scores. Paired t tests were computed for each of the four Vineland scoring methods to determine which one showed the greatest sensitivity to change.

To determine whether certain child characteristics were predictive of skill development, prediction equations were developed to assess whether baseline characteristics were associated with change in adaptive behavior. The predictors were (1) child's chronological age, (2) child's assessed adaptive skill in that domain at baseline, (3) cognitive ability (functional level); (4) ADI-R score on Social Interaction, and (5) ABC-Irritability score. The clinical relevance of the assessed changes in adaptive skill was examined through three different methods: computed effect size estimates (change [pretest/posttest]/pooled SD), gain in age-equivalent months, and the computation of growth indices based on expected adaptive skill development. Specifically, each child's observed adaptive behavior growth was compared to his or her projected growth established at baseline to determine whether the observed gains were greater than the expected change caused by the passage of time alone. An adaptive behavior index (ABI) was derived for each child using the formula

$$\left[\frac{AE_{(EP)}}{CA_{(EP)}} \times 100 \right] - \left[\frac{AE_{(BL)}}{CA_{(BL)}} \times 100 \right] \quad [1]$$

where AE is age-equivalent, CA is chronological age, EP is endpoint, and BL is baseline. This yields an improvement index or a percentage score signaling the observed growth compared to expected growth. Thus, if the child made no gains in his or her

TABLE 2
Change Across Indices of Adaptive Behavior for Risperidone Treatment Responders ($n = 48$)

Domain	Baseline (Mean \pm SD)	Follow-up (Mean \pm SD)	Change (Mean \pm SD)	Effect Size ^a
Communication				
Raw scores	48.58 \pm 26.95	53.79 \pm 28.25	5.21 \pm 9.81*	0.19
Standard scores	43.58 \pm 13.48	45.21 \pm 18.85	1.63 \pm 8.91	0.11
Special norm scores	55.73 \pm 18.93	61.88 \pm 17.73	6.15 \pm 12.47*	0.27
Age-equivalents	31.31 \pm 22.95	36.10 \pm 27.37	4.79 \pm 8.06*	0.20
Daily living skills				
Raw scores	59.15 \pm 24.67	65.92 \pm 24.69	6.77 \pm 12.97*	0.28
Standard scores	39.42 \pm 18.06	40.38 \pm 18.11	0.96 \pm 10.35	0.06
Special norm scores	52.88 \pm 20.37	60.73 \pm 20.08	7.85 \pm 13.84*	0.36
Age-equivalents	37.58 \pm 17.13	42.00 \pm 18.43	4.42 \pm 8.62*	0.27
Socialization				
Raw scores	39.42 \pm 15.77	47.69 \pm 17.65	8.27 \pm 10.69*	0.47
Standard scores	48.67 \pm 9.78	50.50 \pm 12.94	1.83 \pm 9.64	0.14
Special norm scores	50.77 \pm 20.29	61.69 \pm 20.39	10.92 \pm 16.07*	0.49
Age-equivalents	21.94 \pm 13.02	29.73 \pm 18.29	7.79 \pm 9.68*	0.45
Composite^b				
Standard scores	42.35 \pm 15.79	42.06 \pm 13.53	-0.29 \pm 12.53	-0.02
Special norm scores	58.19 \pm 17.24	65.81 \pm 16.79	7.62 \pm 10.85*	0.36
Age-equivalents	30.85 \pm 16.17	36.52 \pm 19.24	5.67 \pm 6.81*	0.33

Note: Data are reported only on those subjects with scores for both time points available.

^a Effect size = change (endpoint - baseline)/baseline SD ($n = 101$).

^b Composite score is derived from the three domain scales and has no raw score value.

* $p < .01$.

ABI, the result would be zero and if observed growth exceeded growth expected with the passage of time, the result would be a positive value. For example, if a 10-year-old child (120 months) earns an age-equivalent of 60 months at baseline and gains five age-equivalent over a 6-month treatment period, his or her improvement index would be

$$\left(\left[\frac{65}{126} \times 100 \right] - \left[\frac{60}{120} \times 100 \right] \right) = .59 \quad [2]$$

RESULTS

Table 1 shows the descriptive baseline data for the entire sample of 101, the 63 subjects who entered the extension, and the 48 who had usable endpoint Vineland data. The distribution of baseline data for socialization standard scores and age-equivalents, as well as adaptive behavior composite scores, was somewhat unevenly distributed, with many relatively low scores. Overall, the profile of Vineland scores for the full sample at baseline is consistent with profiles previously reported for children with autism. Examination of age-equivalents demonstrates a relative strength in daily living skills (mean = 38 ± 17 months), a more severe deficit in socialization (mean = 25 ± 18 months), and intermediate scores in communication (mean = 34 ± 24 months). Bivariate correlations, conducted to examine relationships among Vineland scores and other baseline indicators, indicated that across all four score types (raw, standard, special norm percentiles, and age-equivalents), Vineland scores were most strongly correlated with chronological age (e.g., composite standard score and age, $r = -0.48, p < .01$; composite age-equivalent and age, $r = 0.37, p < .01$). In addition, the correlation between Vineland composite standard scores and ABC-inappropriate speech scores was significant ($r = 0.27, p < .01$). The significant correlation between inappropriate speech and Vineland communication ($r = 0.35, p < .01$) may explain this finding. No other significant correlations were seen.

When the subjects who continued into the 4-month extension phase ($n = 63$) were compared to those who exited the study ($n = 38$) on baseline indicators, the two groups differed only in terms of Vineland socialization raw scores ($t = 2.39, p = .019$) and socialization age-equivalents ($t = 2.44, p = .017$). Subjects who exited the study before the extension had a mean socialization age-equivalent score of 30 months (± 22), compared with 22 months (± 13) for the responders.

The Vineland as a Measure of Treatment Outcome

Change in adaptive behavior from baseline to follow-up was assessed in 48 subjects with full data. Paired t tests, with overall α set at .01 to protect the error rate from inflation, indicated that for each of the three adaptive behavior domains (communication, daily living skills, and socialization), follow-up scores were higher for raw scores, special norm scores, and age-equivalent scores. Standard scores did not show improvement in any of the domains or in the derived Adaptive Behavior Composite ($t_{47} = 0.161, p = .873$).

Although the special norm score effect sizes are consistently larger, this may be a measurement artifact. As shown by Carter et al. (1998), small increases in raw scores can translate into large jumps in special norm percentile rank. For example, if a verbal 8-year-old raises his or her raw score on the communication domain from 33 to 37, his or her special norm percentile rank will improve from 10 to 20. Thus, we chose raw scores and age-equivalents as the criterion measures in the prediction equations.

Multivariate prediction equations were developed for each of the adaptive behavior domains with the following baseline predictors: chronological age, domain score at baseline (raw or age-equivalent), functional level (moderate to profound mental retardation versus mild retardation to average ability), ADI-R Social Interaction score, and ABC-Irritability score. When predicting change in raw scores, none of the prediction equations were statistically significant (communication change: $F_{5,42} = 0.79, R^2 = 0.09$; daily living skills change: $F_{5,42} = 0.72, R^2 = 0.08$; socialization change: $F_{5,42} = 0.04, R^2 = 0.005$). Using change in age-equivalents as the dependent variable, the model predicting communication change was significant ($F_{5,42} = 4.15, p < .01 [R^2 = 0.33]$). The two significant baseline predictors were chronological age ($\beta = -.49, p < .01$) and communication age-equivalent ($\beta = .25, p < .001$). Younger children and those with better developed communication skills at baseline were found to make greater gains in communication with treatment, as measured with age-equivalent scores. The prediction equations for daily living skills and socialization age-equivalent growth were not significant.

As shown in Table 2, computed effect sizes ranged from not meaningful to small/moderate (Borenstein

et al., 2001) for the gains observed across Vineland raw scores, special norm percentile ranks, and age-equivalents. Examination of the age-equivalent change scores shows developmental progress across all domains as well as the composite index and can be used to assess children's rate of growth over time. Over an average of 7 months, the children gained about 5 months in communication and daily living skills domains. In the socialization domain, the gain was closer to 8 months. Such absolute change indices, however, do not take into consideration the child's predicted development (based on baseline performance).

Thus, to determine whether the gains seen in adaptive behavior were greater than would be expected with the passage of time alone, an ABI was derived for each child using the formula provided. Based on these indices, children showed an average $3.5\% \pm 7.82\%$ improvement in overall adaptive behavior. This is higher than expected based on the ratio of age-equivalent to chronological age (i.e., expected growth rate) at baseline. There was a fair degree of variability in derived behavior improvement indices, ranging from -10.95% to 24.18% . Comparison of groups above and below the median split (at 2.72) indicated that the children who made large gains did not differ from those who made smaller gains or regressed. Adaptive behavior improvement indices for each of the domains were positive: communication, $2.60 \pm 8.29\%$; daily living skills, $2.02\% \pm 10.07\%$; and socialization, $6.21\% \pm 10.43\%$. It appears that each adaptive behavior domain contributed to the overall change observed, based on correlations between domain ABIs and the composite ABI: communication, $r = 0.48$, $p < .005$; daily living skills, $r = 0.61$, $p < .001$; and socialization $r = 0.70$, $p < .001$.

Finally, to determine to what degree the observed gains in adaptive behavior may be linked to decreased levels of aggression, the target behavior of the risperidone treatment in the original study, bivariate correlations between change in the ABC-Irritability subscale from baseline to endpoint and changes in raw scores across Vineland domains were made. Correlations were modest and not significant: communication, $r = -0.12$; daily living skills, $r = -0.17$; and socialization, $r = -0.26$. This suggests that large reductions in aggression were not associated with large gains in adaptive functioning.

DISCUSSION

Deficits in adaptive behavior are characteristic of children with autism. Indeed, adaptive functioning scores as measured by the Vineland are a full SD lower than IQ scores in this population (Paul et al., 2004). Consistent with previous studies (Bolte and Poustka, 2002; Carter et al., 1998), age-equivalent scores in this sample show disability across domains, with a relative "strength" in daily living skills and a deficit in socialization.

To determine whether reduction in serious behavior problems with 6 months of risperidone treatment would be accompanied by improved adaptive functioning, we examined four methods for scoring the Vineland, including raw scores, standard scores, special norm scores, and age-equivalent scores, to ascertain the most sensitive method of detecting change. First, children who showed a positive response to risperidone generally manifested increases in adaptive performance regardless of functional level, although younger children with better communication skills tended to make greater gains in terms of communication age-equivalent scores. Second, adaptive behavior growth could only be detected using raw scores, age-equivalent scores, and special norm percentile ranks, not standard scores. Although the observed change is greatest for the special norm scores, this finding may overestimate the positive change in this sample. Carter et al. (1998) developed these norms to aid clinicians in setting realistic treatment goals for individual patients, not for evaluating change in group-design studies. Small to medium effect sizes were observed for both the raw scores and age-equivalent scores across domains, indicating that these two indices are sensitive to change and less vulnerable to the over- or underestimation of change associated with special norm or standard scores, respectively. Given the ease of interpreting gains in age-equivalent scores over time, they appear to be superior for measuring skill growth with treatment.

During a period of 6 to 8 months, subjects gained almost 5 months in communication and daily living skills, and nearly 8 months in socialization. These estimates are similar to those obtained by Charman et al. (2004), who reported a gain of 10 months in communication and 9 in both daily living skills and socialization during an 11-month period using the Vineland-Screener version (Sparrow, 2000). These

gains were observed in children with autism (mean age of 5 years, 11 months) who participated in specialized schools for children with autism (Charman et al., 2004). Harris et al. (1995) reported an even higher rate of improvement in 20 preschoolers in a university-based intensive educational program—27 months in Communication, 17 in Daily Living Skills, and 20 in Socialization during a 20-month time period. As in our study, these earlier studies did not include control groups for comparison.

Our sample differs from the samples described by Charman et al. (2004) and Harris et al. (1995). First, our sample included children with high levels of aggression, tantrums, and self-injury. The sample of Harris et al. (1995) comprised children with mild to moderately severe autism enrolled in a special school for children with autism. The subjects of Charman et al. (2004) were enrolled in schools serving children with autism. Thus, although the samples in these studies probably included some children with behavioral problems, they were not selected for such behavior. Second, the children in our sample were older than those in the Charman et al. study (by about 3 years) and the Harris et al. study (by almost 5 years). Changes in adaptive behavior growth trajectories in children with autism tend to be greater in early childhood and often level off in later childhood (Harris et al., 1995). In older children with autism, adaptive skills generally do not keep pace with the passage of time. Subsequently, standard scores on the Vineland decline with age (Carter et al., 1998; Fisch et al., 2002). Therefore, showing improvement in adaptive functioning in this older sample of children with serious behavioral problems is remarkable and unexpected. The children in this sample demonstrated a 3.5% improvement in their overall ABI from baseline, a >6% improvement in socialization, 2.6% in communication, and 2.02% in daily living skills. Because relatively few studies have assessed growth in adaptive behavior with treatment in comparison to expected growth with time, it is difficult to interpret the meaning of this improvement. Using a similar approach in 35 children with autism (mean age 7.11 ± 2.6 years) who were not provided with specific interventions over a 3-year longitudinal study (Tager-Flusberg, personal communication, 2005) revealed the following ABIs, computed with the formula given: communication (-0.20%), daily living skills (-4.60%), and socialization (-3.08%). Based on these data, we

conclude that without treatment, children with autism do not improve their adaptive behavior growth rate and may in fact regress. Replication of these findings with larger samples is needed. It is also worth noting that the greatest gain in skill development in this sample was in the area of socialization, a core deficit in autism.

Although there was no control group in the 4-month open-label extension, there is reason to believe that the observed gains seen in adaptive behavior may be caused by risperidone treatment. First, the response to drug treatment was rigorously established in this sample by other measures and placebo control. Second, there was a high rate of relapse in subjects assigned to gradual placebo substitution under double-blind conditions (RUPP Autism Network, 2005). Alternatively, many of these children were in special education programs, which may have contributed to the observed gains. Nevertheless, it could be argued that risperidone made the children more available for these other ongoing interventions. The most common complaint from parents in this sample was tantrums (Arnold et al., 2003). Based on parental response during the double-blind phase, risperidone was highly effective for this behavior. Perhaps the reduction in tantrums sets the stage for better compliance with routine demands, improved functional communication, and better social functioning. Modest, although not statistically significant, correlations between reduction in problem behavior and adaptive skill growth were seen. Future studies could examine this proposed mechanism through comparison of drug-only versus drug plus behavioral treatment. Although more study is needed to determine whether these observed gains are related to medication, it is clear that children with autism have the capacity to develop adaptive skills and to alter their flat developmental trajectory with treatment.

Limitations

Because of the small sample, we could not identify specific child or environmental characteristics that were associated with adaptive skill growth. In addition, because this sample was selected for severe behavioral problems, findings may not generalize to other less impaired samples. Third, there was no placebo control for the entire 6-month duration. Therefore, we cannot attribute the observed gains to risperidone with certainty. All of the subjects in this sample showed a

positive response to treatment with risperidone, suggesting that the adaptive skill gains could be an indirect effect of drug treatment. Comparing their Vineland change with that of children who did not improve significantly with risperidone would be useful. Finally, 6 months of treatment is relatively short in the context of a child's overall development. Studies evaluating the impact of interventions, both pharmacological and psychosocial, on adaptive behavior using the scoring methods outlined in this article over longer time periods would be useful.

Clinical Implications

Children with autism accompanied by severe behavior problems can achieve clinically meaningful growth in adaptive skills from effective pharmacological treatment. The Vineland Adaptive Behavior Scales can be used to evaluate change, but standard scores may underestimate improvement. Standard scores based on national norms are needed to document the presence of mental retardation and are useful for characterization. Because of problems with lack of variability and basal effects, however, the usefulness of standard scores for growth evaluation is limited. Therefore, both raw scores and age-equivalents seem useful because they are sensitive to change over time. Age-equivalent scores can also be useful in providing growth indices over time. Clinicians can derive an adaptive behavior improvement index, using the formula provided, to determine the impact of treatment on a given child.

Disclosure: Dr. Scabill has affiliations with Janssen Pharmaceutica, Pfizer and Bristol-Myers Squibb. Dr. Aman has affiliations with Janssen Pharmaceutica, Eli Lilly, Forest Labs, and Abbott. Dr. Arnold has affiliations with Eli Lilly, McNeil, Novartis, Noven, Shire, Sigma Tau, and Targacept. Dr. McDougle has affiliations with AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Janssen Pharmaceutica, PediaMed Pharmaceuticals, and Pfizer, Inc. Dr. McCracken has affiliations with Janssen Pharmaceutica, Eli Lilly, Abbott, Bristol-Myers Squibb, Shire, Wyeth, Pfizer, Cephalon, and McNeil. Dr. Posey has affiliations with Eli Lilly, Pfizer, and Janssen. Drs. Cicchetti and Sparrow receive royalties from sales of the Vineland Adaptive Behavior Scales from AGS Publishing. The other authors have no financial relationships to disclose.

REFERENCES

- Aman MG, Singh NN, Stewart AW, Field CJ (1985a), Psychometric characteristics of the Aberrant Behavior Checklist. *Am J Ment Defic* 89:492-502
- Aman MG, Singh NN, Stewart AW, Field CJ (1985b), The Aberrant Behavior Checklist: a behavior rating scale for the assessment of treatment effects. *Am J Ment Defic* 89:485-491
- Arnold LE, Vitiello B, McDougle CJ, (2003), Parent-defined target symptoms respond to risperidone in RUPP autism study: customer approach to clinical trials. *J Am Acad Child Adolesc Psychiatry* 42: 1443-1450
- Bibby P, Eikeseth S, Martin NT, Mudford OC, Reeves D (2002), Progress and outcomes for children with autism receiving parent-managed intensive interventions. *Res Dev Disabil* 23:81-104
- Bolte S, Poustka F (2002), The relation between general cognitive level and adaptive behavior domains in individuals with autism with and without co-morbid mental retardation. *Child Psychiatry Hum Dev* 33:165-172
- Borenstein M, Rothstein H, Cohen J (2001), *Power and Precision: A Computer Program for Statistical Power Analysis and Confidence Intervals*. Englewood, NJ: Biostat
- Brown EC, Aman MG, Havercamp SM (2002), Factor analysis and norms on parent ratings with the Aberrant Behavior Checklist: community for young people in special education. *Res Dev Disabil* 23:45-60
- Burack JA, Volkmar FR (1992), Development of low- and high-functioning autistic children. *J Child Psychol Psychiatry* 33:607-616
- Carter AS, Volkmar FR, Sparrow SS et al. (1998), The Vineland Adaptive Behavior Scales: supplementary norms for individuals with autism. *J Autism Dev Disord* 28:287-302
- Charman T, Howlin P, Berry B, Prince E (2004), Measuring developmental progress of children with autism spectrum disorder on school entry using parent report. *Autism* 8:89-100
- Eikeseth S, Smith T, Jahr E, Eldevik S (2002), Intensive behavioral treatment at school for 4- to 7-year-old children with autism. *Behav Modif* 26:49-68
- Fisch GS, Simensen RJ, Schroer RJ (2002), Longitudinal changes in cognitive and adaptive behavior scores in children and adolescents with fragile X mutation or autism. *J Autism Dev Disord* 32:107-114
- Freeman BJ, Ritvo ER, Yokota A, Childs J, Pollard J (1988), WISC-R and Vineland Adaptive Behavior Scale scores in autistic children. *J Am Acad Child Adolesc Psychiatry* 27:428-429
- Gillham JE, Carter AS, Volkmar FR, Sparrow SS (2000), Toward a developmental operational definition of autism. *J Autism Dev Disord* 30: 269-278
- Harris SL, Handleman JS, Belchic J, Glasberg B (1995), The Vineland Adaptive Behavior Scales for young children with autism. *Spec Serv Schools* 10:45-54
- Kraijer D (2000), Review of adaptive behavior studies in mentally retarded persons with autism/pervasive developmental disorder. *J Autism Dev Disord* 30:39-47
- Lord C, Rutter M, LeCouteur A (1994), Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *J Autism Dev* 24:659-685
- Marshburn EC, Aman MG (1992), Factor validity and norms for the Aberrant Behavior Checklist in a community sample of children with mental retardation. *J Autism Dev Disord* 22:357-373
- Mullen E (1995), *The Mullen Scales of Early Learning*. Circle Pines, MN: American Guidance Service
- Panerai S, Ferrante L, Zingale M (2002), Benefits of the treatment and education of autistic and communication handicapped children (TEACCH) program as compared with a non-specific approach. *J Intellect Disabil Res* 46:318-327
- Paul R, Miles S, Cicchetti D et al. (2004), Adaptive behavior in autism and pervasive developmental disorder-not otherwise specified: microanalysis of scores on the Vineland Adaptive Behavior Scales. *J Autism Dev Disord* 34:223-228
- Research Units on Pediatric Psychopharmacology Autism Network (2002), Risperidone in children with autism and serious behavioral problems. *N Engl J Med* 347:314-321
- Research Units on Pediatric Psychopharmacology Autism Network (2005), Risperidone for the core symptom domains of autism: results from the study by the autism network of the research units on pediatric psychopharmacology. *Am J Psychiatry* 162:1142-1148
- Roid GH, Miller LJ (1997), *Leiter International Performance Scale-Revised*:

- Examiner's Manual. Leiter International Performance Scale-Revised.* Wood Dale, IL: Stoelting
- Scahill L, Lord C (2004), Subject selection and characterization in clinical trials in children with autism. *CNS Spectrums* 9:22–32
- Scahill L, McCracken J, McDougle CJ et al. (2001), Methodological issues in designing a multisite trial of risperidone in children and adolescents. *J Child Adolesc Psychopharmacol* 11:377–388
- Schatz J, Hamdan-Allen G (1995), Effects of age and IQ on adaptive behavior domains for children with autism. *J Autism Dev Disord* 25:51–60
- Smith T, Buch GA, Gamby TE (2000a), Parent-directed, intensive early intervention for children with pervasive developmental disorder. *Res Dev Disabil* 21:297–309
- Smith T, Groen AD, Wynn JW (2000b), Randomized trial of intensive early intervention for children with pervasive developmental disorder. *Am J Ment Retard* 105:269–285
- Sparrow S (2000), *Vineland Adaptive Behavior Scales-Screener*. New Haven, CT: Yale Child Study Center
- Sparrow S, Balla D, Cicchetti D (1984), *Vineland Adaptive Behavior Scales-Survey Edition*. Circle Pines, MN: American Guidance Service
- Stone WL, Ousley OY, Hepburn SL, Hogan KL, Brown CS (1999), Patterns of adaptive behavior in very young children with autism. *Am J Ment Retard* 104:187–199
- VanMeter L, Fein D, Morris R, Waterhouse L, Allen D (1997), Delay versus deviance in autistic social behavior. *J Autism Dev Disord* 27: 557–569
- Volkmar FR, Carter A, Sparrow SS, Cicchetti DV (1993), Quantifying social development in autism. *J Am Acad Child Adolesc Psychiatry* 32: 627–632
- Wechsler D (1989), *Manual for the Wechsler Preschool and Primary Scale for Children-Revised*. San Antonio, TX: The Psychological Corporation
- Wechsler D (1991), *Manual for the Wechsler Intelligence Scale for Children-Third Edition*. San Antonio, TX: The Psychological Corporation
- Wolery M, Garfinkle AN (2002), Measures in intervention research with young children who have autism. *J Autism Dev Disord* 32:463–478

Are Language Barriers Associated With Serious Medical Events in Hospitalized Pediatric Patients? Adam L. Cohen, MD, MPH, Frederick Rivara, MD, MPH, Edgar K. Marcuse, MD, MPH, Heather McPhillips, MD, MPH, Robert Davis, MD, MPH

Objective: Language barriers may lead to medical errors by impeding patient-provider communication. The objective of this study was to determine whether hospitalized pediatric patients whose families have language barriers are more likely to incur serious medical errors than patients whose families do not have language barriers. *Methods:* A case-control study was conducted in a large, academic, regional children's hospital in the Pacific Northwest. Case patients ($n = 97$) included all hospitalizations of patients who were younger than 21 years and had a reported serious medical event from January 1, 1998, to December 31, 2003. Control patients ($n = 475$) were chosen from hospitalizations without a reported serious medical event and were matched with case patients on age, admitting service, admission to intensive care, and date of admission. The main exposure was a language barrier defined by self- or provider-reported need for an interpreter. Serious medical events were defined as events that led to unintended or potentially adverse outcomes identified by the hospital's quality improvement staff. *Results:* Fourteen (14.4%) of the case patients and 53 (11.2%) of the control patients were assigned an interpreter during their hospitalization. Overall, we found no increased risk for serious medical events in patients and families who requested an interpreter compared with patients and families who did not request an interpreter (odds ratio: 1.36; 95% confidence interval: 0.73–2.55). Spanish-speaking patients who requested an interpreter comprised 11 (11.3%) of the case patients and 26 (5.5%) of the control patients. This subgroup had a twofold increased risk for serious medical events compared with patients who did not request an interpreter (odds ratio: 2.26; 95% confidence interval: 1.06–4.81). *Conclusions:* Spanish-speaking patients whose families have a language barrier seem to have a significantly increased risk for serious medical events during pediatric hospitalization compared with patients whose families do not have a language barrier. **Pediatrics** 2005;116:575–579.