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Examination of Aggression and Self Injury in Children with Autism Spectrum Disorders and Serious Behavioral Problems

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Synopsis

This study identified subtypes of aggression in a sample of 206 children (174 boys, 32 girls) with autism spectrum disorder (ASD) who participated in two risperidone trials conducted by the Research Units on Pediatric Psychopharmacology (RUPP) Autism Network. The classification of aggression subtypes was based on a review of brief narratives documented at baseline. The narratives were derived from a parent interview about the child's two most pressing problems. Five subtypes of aggression emerged: hot aggression only, cold aggression only, self-injurious behavior (SIB) only, aggression and SIB, and non-aggressive. The aggression and SIB group had the highest proportion of children with IQ below 70. Children in the hot aggression group were slightly younger and had higher scores on the ABC-Irritability subscale than the non-aggression group. The SIB only group had the highest ABC-Irritability score. All groups showed a high rate of positive response to risperidone with no differences across subtypes. These study findings extend our understanding of aggression in ASD and may be useful to guide further study on biological mechanisms and individualized treatment in ASD.

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Introduction

Pervasive Developmental Disorders (PDDs) are lifelong, neurodevelopmental conditions characterized by impairments in social interaction and communication skills, as well as repetitive behavior and unusual preoccupations.¹ In DSM-V, the former diagnostic classifications of Autistic Disorder, Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) and Asperger's Disorder will be collapsed into a single category called Autism Spectrum Disorder (ASD), reflecting their common features and potentially shared etiologies. Recent estimates of prevalence indicate that ASDs affect as many as 110 per 10,000 children.²

In addition to the core symptoms, children with ASDs may exhibit other problems including tantrums, aggression, self-injury, hyperactivity, anxiety or rapid changes in mood.³ The prevalence of aggressive behavior in this population varies widely depending on the source of sample and method of assessment.⁴⁻⁸ Aggression, whether directed toward the self or others, may result in injury and distress for the child and caregivers. Not surprisingly, aggression is a common chief complaint of parents and educators.⁹ Behavioral treatment of aggression can be challenging, expensive and often requires expertise that may not be available in all communities.¹⁰ Although two atypical antipsychotic medications, risperidone and aripiprazole, are FDA-approved for the treatment of irritability (tantrums, aggression and self-injury), these medications are associated with short- and long-term adverse effects.^{5,11-13} In addition, medication withdrawal of risperidone after six months of effective treatment resulted in the rapid return of disruptive behaviors.¹⁴

Pharmacological studies on the treatment of aggression generally do not discriminate between types of aggressive behaviors.^{12,15,16} The randomized, controlled risperidone and aripiprazole trials that led to FDA approval enrolled children with autistic disorder with any combination of tantrums, aggression and self-injury as measured by the Aberrant Behavior Checklist (ABC) Irritability subscale.^{12,17-19} Although the term "irritability" implies an affective component, these studies did not evaluate the context of the tantrums, aggression and self-injury. Behaviorists, on the other hand, are keenly focused on the context or the "function" of the behavior.²⁰ For example, the function of an aggressive outburst may be to obtain a tangible object (food or a preferred object) or to escape an environmental demand (getting dressed). Self-injury (aggression directed at the self) occurs in some children with ASDs and may occur with or without externally directed aggression. Functional analysis is also relevant to self-injurious behavior.²⁰⁻²² The repetitive motoric nature of self-injurious behavior (SIB) in some children suggests that it may differ from other types of aggressive behavior.²⁰

In the broader field of behavioral science, research has focused on subtypes of aggression in order to understand the underlying mechanisms.²³ The classical taxonomy originating from animal research distinguishes between predatory (proactive) and affective (reactive) aggression. The characteristics of reactive and proactive aggression have been studied in animal models and in humans.^{23,24,25} Proactive aggression ("cold aggression") is intended to achieve a desired reward and in its classic form occurs without anger or prior provocation.^{23,26,27} Reactive, or "hotheaded" aggression, occurs in response to a perceived

or real provocation and is often impulsive.^{23,24,25} However, these “subtypes” of aggression may not be mutually exclusive.^{23,28} In ASD, for example, the child who is intent on obtaining a preferred object, may over-react and become aggressive in the fervent effort to obtain the object.

The reactive and proactive subtypes of aggression have been studied in the general pediatric population and, to a lesser extent, in clinical samples.^{29,30} To date, most studies of aggression in clinical samples have focused on children with attention deficit hyperactivity disorder, oppositional defiant disorder and conduct disorder.^{25,31,32} Research on aggression subtypes in children with ASDs is limited.^{7,8} In a sample of 1,380 children with ASD ages 4 to 17 years from the Simons Simplex data base, Kanne and Mazurek (2011) estimated the prevalence of current aggression at 35%. This estimate was based on a single item from the Autism Diagnostic Interview – Revised. Parents were asked to rate aggression on a four-point scale (0= none; 1=mild; 2=moderate; 3=severe). The 35% estimate reflects the percentage of children rated 2 or 3 on this item. A secondary analysis of the Autism Treatment Network data (N=1,584; age 2 to 17 years) estimated a prevalence of aggression of 53.7% based on a “yes” or “no” response from parents on a single question about aggression. This higher rate likely includes children with “mild” aggression, who were not counted in the estimate of 35% from the Simons Simplex data base. These reports did not attempt to classify the types of aggression or SIB in these samples of children with ASD.

In this analysis we examine aggressive behavior in children who participated in the two risperidone trials conducted by the Research Units on Pediatric Psychopharmacology (RUPP) Autism Network.^{12,15}

First, we classified subtypes of aggression and self-injury based on the parents’ chief complaint documented at baseline. Second, we examined differences in these subtypes by comparing demographic and clinical characteristics by subtype. Finally, we explored treatment response to risperidone across subgroups.

Methods

Setting and Subjects

Subjects were enrolled in one of two randomized clinical trials conducted by the RUPP Autism Network. The first study was an 8-week, double-blind, placebo-controlled trial of risperidone in 101 children 5 – 17 years old with Autistic Disorder. The second study was a 24-week randomized trial of risperidone only versus risperidone plus parent training in 124 children with ASDs from 4 – 13 years of age. Medication dosing and blinded assessments in these two studies were virtually identical for the first eight weeks, which permitted comparison of baseline characteristics and outcomes across the two trials. Both studies required the presence of serious behavioral problems such as tantrums, aggression, or self-injury in various combinations, as evidenced by a score of 18 or higher on the Aberrant Behavior Checklist-Irritability subscale (ABC-I). This score is approximately 1.3 standard deviation units above the population mean for individuals with developmental disabilities.^{33,34}

The two trials included a total of 225 subjects (187 boys, 38 girls). Subjects in both studies were free of serious medical disorders or other psychiatric disorders requiring medication. All children were drug-free for 7 to 28 days, depending on the drug (7 days for stimulants and alpha 2 agonists, 28 days for fluoxetine or antipsychotics), before enrollment. Thus, with the exceptions of including subjects with broader ASD diagnosis and narrower age range in the second trial, the two studies had essentially the same entry criteria. The design of each trial, the risperidone dosing schedule and the characteristics of the samples are described in detail in prior reports.^{12,15,35,36} Both projects were approved by Institutional Review Boards (IRB) at participating clinical sites. Parents or legal guardians of all child participants provided written informed consent.

Measures

Prior to randomization, participants in both trials received a comprehensive psychiatric and medical evaluation (including electrocardiogram, vital signs, medical history, physical examination, and routine laboratory tests). Diagnoses of Autistic Disorder, Asperger's Disorder, and PDD-NOS were based on a clinical evaluation according to DSM-IV³⁷ or DSM-IV-TR¹ criteria. The diagnoses were further supported by the Autism Diagnostic Interview-Revised (ADI-R).³⁸ The following assessment battery was used to confirm eligibility, characterize the sample and establish baseline severity.

Parent Target Problems—(PTP) At baseline the clinician asks parents to identify one or two chief complaints concerning their child's behavior. Parents are then asked to describe the frequency, duration (or time spent), intensity and impact of the behavior on daily function or family life. This description was documented in a brief narrative at baseline, which was used as baseline for an outcome measure of change over time.³⁹ However, for classifying aggression and self-injurious behavior (SIB) in this study, we used only the baseline narratives from these two trials.

Intellectual Functioning—Based on the child's capacity to complete the test, several different intelligence tests were used including: Stanford Binet-V⁴⁰, Wechsler Intelligence Scales for Children-III⁴¹, Leiter International Performance Scale-Revised⁴², Mullen Scales of Early Learning⁴³, Slosson Intelligence Test⁴⁴ and Wechsler Preschool and Primary Scale of Intelligence-Revised.⁴⁵ Because several different tests were used, children were classified into two IQ categories: < 70 or ≥ 70.

Clinical Global Impressions Scale (CGI)—The CGI-Severity scale (CGI-S) is a clinician-rated 7-point measure of overall severity, ranging from 0 (normal) to 7 (extreme).⁴⁶ A score of 4, reflecting moderate or greater disturbance, was required for study inclusion. The CGI-Improvement scale (CGI-I) is a clinician-rated scale designed to assess change from baseline, based on all available sources of information. Scores range from Very Much Improved (1) through No Change (4) to Very Much Worse (7). In keeping with convention, a score of Much Improved or Very Much Improved was used to define positive response.

Autism Diagnostic Interview-Revised (ADI-R)—The ADI-R is a reliable and valid structured parent interview used to support the diagnosis of autistic disorder.^{38,47,48} The interview inquires about reciprocal social interaction, communication, restricted interests and repetitive behavior. In these RUPP Autism Network trials, interviews were administered and scored by clinicians trained to reliability.

Vineland Adaptive Behavior Scales—The Vineland is a semi-structured parent interview designed to assess functioning in three domains: communication, daily living skills and socialization. This instrument is a standard assessment tool and has demonstrated excellent reliability and validity.⁴⁹

Aberrant Behavior Checklist (ABC)—The ABC is a 58-item rating scale that is completed by a parent or teacher. The ABC has normative data in children with developmental disabilities³³ and is sensitive to change in this population.^{12,15} Items are rated on a 4-point scale ranging from 0 (not a problem at all) to 3 (the problem is severe). There are five factor-analyzed subscales: Irritability (15 items), Social Withdrawal (16 items), Stereotypic Behavior (7 items), Hyperactivity (16 items) and Inappropriate Speech (4 items). The Irritability subscale surveys aggression, self-injury, tantrums and unstable mood. Scores range from 0 to 45; higher scores indicate greater levels of symptom severity.³⁴

Children's Yale-Brown Obsessive-Compulsive Scale for Pervasive Developmental Disorders (CYBOCS-PDD)—The CYBOCS is a semi-structured, clinician-rated interview designed to assess the current severity of obsessions and compulsions in youth with Obsessive Compulsive Disorder.⁵⁰ In the risperidone trials, the CYBOCS was modified for use in children with ASDs.⁵¹ The modified CYBOCS does not include the checklist or severity scales for obsessions, but retains the checklist and severity scales for compulsions. The five severity items include: Time Spent, Interference, Distress, Resistance and Degree of Control, each rated from 0–4. This scale yields a single total score from 0–20.⁵¹

Procedures

Classification of Parent Target Problems—Coding proceeded in several steps. First, two coders (DC, LS) examined 20 Parent Target Problems (PTPs) from 10 randomly selected cases. By consensus, these raters proposed six categories and then independently classified all available baseline PTPs into one of these six categories. Disagreements were resolved by consensus.

Given that each subject had two PTPs, a subject could have 0, 1, or 2 problems with aggression or SIB. To create mutually exclusive groups, children were classified as follows: 1) hot aggression only (one PTP indicated hot aggression, the other did not involve aggression or SIB); 2) cold aggression only (one PTP indicated cold aggression, the other did not involve aggression, SIB or tantrums); 3) SIB only; 4) hot and cold aggression (one PTP reflected hot aggression, the other reflected cold aggression); 5) aggression and SIB (one PTP reflected aggression, the other reflected self-injury); 6) non-aggression (neither PTP reflected aggression or SIB, e.g., tantrums not involving aggression or SIB). Table 1

presents examples of Parent Target Problems at baseline and their classification in this study. These classifications were based on inferences by the study raters (DC, LS). Parents were not directly asked to comment on the classification of hot or cold aggression.

Analytic Strategy

Demographic characteristics (age, gender, race and ethnicity, and educational placement) and clinical characteristics (ASD diagnosis; IQ category: < 70 or ≥ 70; scores on the CGI-S, Vineland, ADI-R, ABC and CYBOCS-PDD; heart rate and blood pressure) were evaluated in the available sample.

Inter-rater agreement for the independent coding of the individual PTPs (two per child) was evaluated with Cohen's kappa, which corrects for chance.⁵² Once the frequency of PTP categories was established, subtypes were compared on demographic and clinical characteristics. Continuous variables were evaluated by ANCOVA (controlling for IQ) across aggression subtypes. Pairwise differences were investigated using Tukey post hoc comparisons. Chi square tests were used for categorical variables. A repeated measures mixed model was used to determine the main effects of Group (aggression subtype) and Time (baseline and Week 8) and the Group*Time interaction on the ABC-Irritability subscale in risperidone-treated subjects (i.e., subjects on placebo in the first RUPP trial were not included in the analysis). To assess treatment response by aggression subtype on the CGI-I (positive response = score of Much Improved or Very Much Improved) at Week 8, we conducted a series of pairwise comparisons. The hot aggression, cold aggression, SIB, aggression + SIB, and hot aggression + hot SIB groups were each compared to the non-aggression group. These analyses also did not include subjects assigned to placebo in the first trial.

Results

Sample Characteristics

Due to missing or incomplete Parent Target Problems (PTPs) for 19 subjects at baseline, the present analyses included 206 children (174 boys, 32 girls). Table 2 presents demographic and clinical characteristics for this sample.

Inter-rater agreement on the classification of aggression subtypes was good (kappa= 0.77 [95% CI, 0.71, 0.84]). Table 3 presents the frequency of the aggression subtypes: hot aggression only (n=65), cold aggression only (n=32), SIB only (n=33), aggression + SIB (n=17), nonaggression (n=53). Children with reported hot *and* cold aggression were excluded (n=6) from Table 3 and all subsequent analyses owing to the small number and difficulty of placing them in either group.

There were no significant differences on gender ($\chi^2(4,200) = 2.60, p=0.63$), ethnicity ($\chi^2(16) = 18.23, p=0.31$) or ASD diagnosis ($\chi^2(8) = 11.82, p=0.16$) across the five groups (note: the 6 subjects with hot and cold aggression were not included). There were also no group differences in the available physiological measures of heart rate ($F(4,188)=0.80; p=0.53$) and systolic blood pressure ($F(4,179)=0.34; p=0.85$).

Chi square analysis showed group differences by IQ ($\chi^2(4) = 10.06, p < 0.05$). Pair-wise comparisons showed that children in the aggression + SIB group had a higher proportion of children with IQ below 70 (82%) compared to the following groups: hot aggression only (48%, $\chi^2(1) = 6.41, p = 0.01$) the cold aggression only (47%; $\chi^2(1) = 6.30, p = 0.01$) and non-aggression (5%, $\chi^2(4) = 8.11, p < 0.01$). Children with reported SIB only were also more likely to have an IQ below 70 (67%) compared to the non-aggression group (47%; $\chi^2(4) = 3.75, p = 0.05$). Age differed significantly across aggression types ($F(4,199) = 2.42; p = 0.05$). This finding was driven by the marginally younger group with hot aggression (mean 7.29 ± 2.27 years) compared to the non-aggression group (mean 8.61 ± 2.49 years; $p = 0.06$). No other pair-wise comparisons were significant on post-hoc testing.

With adjustment for IQ, the omnibus ANCOVA was significant on the ABC- Irritability subscale ($F(4,180) = 5.11, p < 0.01$). Pairwise comparisons by subtype confirmed that children in the aggression + SIB group had significantly higher ABC Irritability scores (mean 33.00 ± 7.91) than children in the non-aggression group (mean $25.50 \pm 7.00; p < 0.05$). The general pattern suggests that the children with aggression + SIB are more severely affected (see Table 3). After adjusting for IQ, however, other ABC subscales, Vineland scores, CYBOCS-PDD scores, CASI PDD and Anxiety scores were not different across groups.

The rate of positive response to risperidone (CGI-I rating of Much Improved or Very Much Improved) was not significantly different across the five groups ($\chi^2(4) = 1.45; p = 0.84$). Table 4 shows the rate of positive and negative response to risperidone by aggression subtype. In a post hoc analysis, we created a group with hot aggression and hot SIB (defined by SIB occurring in the context of angry outbursts). As shown in Table 4, the positive response to risperidone was high in all groups and there were no significant differences between groups with aggressive behavior, SIB or the combination compared to the non-aggression group.

Figure 1 illustrates the change in ABC Irritability in each of the aggression subtypes (in the risperidone treatment groups). The mean scores in the placebo group are also shown for comparison. In the risperidone-treated groups, there was a significant effect of Time (baseline vs week 8: $F(1,221) = 144.59; p < 0.01$) and Aggression Group ($F(4,221) = 3.14; p < 0.05$). The Aggression Group*Time interaction was not significant ($F(4,221) = 0.39; p > 0.05$).

Discussion

In this study we attempted to identify subtypes of aggression in a sample of children with ASDs who participated in two NIMH-funded multi-site trials of risperidone conducted by the RUPP Autism Network.^{12,15} The classification of aggression subtypes was based on a semi-structured narrative derived from parent-reported chief complaint at baseline in each study. Five subtypes of aggression emerged: hot aggression only, cold aggression only, SIB only, aggression and SIB, and non- aggression. Approximately 3% of the sample were classified with both hot *and* cold aggression and were dropped from the analysis. The most common subtype of aggression in this sample selected for moderate or greater levels of

irritability was hot aggression. Children in the hot aggression group had higher scores on ABC-Irritability subscale than those without a chief complaint of aggression. Children with aggression and SIB had the highest ABC-Irritability subscale score. Children with IQ below 70 were more likely to show SIB – either alone or in combination with aggression. The hot aggression group was significantly, albeit slightly, younger than the nonaggression group. The percentage rate of positive response to risperidone was not different across groups as measured by a rating of Much Improved or Very Much Improved on the CGI-I. All risperidone-treated groups showed improvement on the ABC-Irritability subscale with no differences across groups. Given the selection criteria and the large treatment effects of risperidone in these trials, the finding of no group differences in clinical response is not surprising.

Our classification of hot aggression, which occurred in the context of tantrums, is conceptually similar to reactive aggression in youth without developmental disabilities.^{26,28,53} Cold aggression in this ASD population, which appears to be driven by interest in a preferred object or escape from routine demand without a report of explosive behavior, could be analogous to proactive aggression.^{26,28,53} However, cold aggression in this sample was a default classification in some cases – i.e., occurring without a report of explosive behavior. This may have resulted in some misclassification. Proactive aggression is also associated with predatory aggression (premeditated acts of coercion, attacks with purpose to steal, or bullying).^{28,54} The degree to which acts of cold aggression are predatory, premeditated or antisocial in children with ASD may be difficult to determine. Thus, cold aggression in ASD may diverge from the traditional construct of proactive aggression. In some children with ASD, cold aggression may be impulsive in nature rather than planned. Moreover, hot and cold aggression may serve similar functions (tangible object or escape from routine demand)– but hot aggression reflects the added problem of poor emotion regulation.

The most severely affected group in this sample included children with aggression and SIB. Not surprisingly, these children were more likely to have intellectual disability, had higher baseline ABC -Irritability scores, and lower Vineland Communication and Vineland Socialization scores. It is reassuring that this severely affected group showed a similar rate of positive response to other aggression subgroups. Indeed, when we defined on a post hoc basis a subgroup of hot aggression and hot SIB, this group also showed a high rate of positive response to risperidone. These results suggest that risperidone is a rather blunt intervention that exerts positive effects in children with ASD with serious behavioral problems in the context of hot aggression, cold aggression and tantrums in the absence of aggression. This runs counter to clinical lore that medication intervention is more likely to be effective for reactive than proactive aggression. The concept has not been carefully tested (even in a *post hoc* manner as we have done) and warrants further empirical evaluation.

Limitations

This study offers new information about subtypes of aggression in children with ASDs, but several limitations should be noted. First, we constructed these subtypes after reviewing written descriptions by clinicians following an open-ended inquiry about the child's two

most important problems. The purpose of documenting the narratives was not focused on classifying subtypes of aggression. If we had engaged clinicians in this endeavor, they may have obtained more or even different information. Thus, although the level of agreement on classification of aggression was high, our method of inquiry may have missed information that could have influenced the classification.

Second, this was a convenience sample with known and unknown biases. The study sample included subjects with serious behavioral problems, which threatens the generalizability of our findings to the wider ASD population. The entry criteria for these two trials required subjects to have elevated scores on the ABC-Irritability subscale. This criterion may have limited the detection of differences by aggression subgroup. A wider sample of children with ASDs with a broader range of behavioral disturbances would be needed to confirm the validity of aggression subtypes in ASD.

Third, the classification strategy used in the current study was intended to create mutually exclusive groups. Although the target problem narratives evaluated here support the existence of aggression subtypes, the narratives only documented two problems. Inquiry about a third problem could have identified a problem in another aggressive subtype and affected classification. Indeed, in typically developing youth and youth with ASD, hot and cold aggression are highly correlated.^{28,55} Thus, the placement of subjects in one or another subtype will result in some misclassification and make it difficult to find differences between groups. A dimensional measure of aggression collected in a larger and more diverse population of children with developmental disabilities would be a way to learn more about the subtypes of aggression in children with ASDs.

Conclusions

The results of this study support, but do not confirm, the subtypes of hot and cold aggression in children with ASDs. These subtypes, which were adapted from previous studies on aggression outside the realm of ASDs, may be useful to guide further study on biological mechanisms and individualized treatment. Overall, however, our data suggest that aggression subtypes respond similarly to treatment with risperidone. Future studies could examine whether targeting the inadequate emotion regulation of children with hot aggression would lead to benefit from less potent medications or behavioral interventions.²⁵

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Abbreviations: Autism and Aggression

NCRR	National Center for Research Resources
ASD	autism spectrum disorder
SIB	self-injurious behavior
RUPP	Research Units on Pediatric Psychopharmacology
PDDs	Pervasive Developmental Disorders
PDD-NOS	Pervasive Developmental Disorder-Not Otherwise Specified
ABC	Aberrant Behavior Checklist
ABC-I	Aberrant Behavior Checklist-Irritability
IRB	Institutional Review Boards
ADI-R	Autism Diagnostic Interview-Revised
PTP	Parent Target Problems
CGI	Clinical Global Impression Scale
CGI-S	Clinical Global Impression Severity Scale
CGI-I	CGI-Improvement scale
ADI-R	Autism Diagnostic Interview-Revised
CYBOCS-PDD	Children's Yale-Brown Obsessive-Compulsive Scale for Pervasive Developmental Disorders

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Key Points

- Aggression and self-injurious behavior are relatively common in children with autism spectrum disorder (ASD) and impair adaptive function.
- Typologies such as proactive (cold) aggression and reactive (hot) aggression have been described, but not previously applied to ASD.
- This study identified subtypes of aggression in a sample of 206 children with ASD (age 5 to 17 years) who participated in two risperidone trials conducted by the Research Units on Pediatric Psychopharmacology Autism Network.
- Five subtypes emerged: hot aggression only, cold aggression only, self-injurious behavior (SIB) only, aggression and SIB, and non-aggression. However, these groups are not mutually exclusive as children may show aggression or SIB in different categories.
- Despite some differences in clinical characteristics across subtypes, all groups showed a positive response to risperidone.

Figure 1.

Table 1

Selected Examples of Parent Target Problems for participants in RUPP* Autism Network risperidone trials

Problem	Description	Impact/Consequences	Classification
Tantrums	Occur at home and school. Behaviors include swearing, destruction of toys, slamming doors, and throwing things. May hit mother or sibling.	Occur 10–15 times per day; lasting 5 to 20 minutes. Parents may have to restrain him to calm him down.	Hot aggression
Impulsive Aggression	Includes pulling at mother's glasses, pulling hair, & hitting (mother or sister). Behavior is unpredictable.	Occurs daily up to 5 times per day. Mother tells him "no" & sends him to the time-out chair.	Cold Aggression
Self-injury	Scratches and bites himself about 3 times per day. Gets upset when he doesn't get his way, or when sitting in time out. Hits his head against the wall.	Daily; makes holes in the walls; leaves marks or draws blood.	SIB (Hot subtype)
Screaming & Outbursts	Has outbursts every day at least once an hour. Subject will have a screaming outburst if he wants something, if he wants someone to leave him alone, and for no apparent reason at times. Only stops if something distracts him.	Episodes last seconds to 10 minutes. Family can only go to places where screaming is acceptable (i.e., Magic Mountain). Behavior interferes with learning.	Non aggression
Impulsiveness	"near constant." Mother says: "hundreds of episodes per day." Behavior is extremely dangerous, as he may dart into the road or bolting in parking lots.	Wearing on the family, hard to do the simplest errands with the child, family avoids taking the child to outings expect grocery store.	Non aggression

* RUPP =Research Units on Pediatric Psychopharmacology

Table 2

Demographic and Clinical Characteristics of all participants in RUPP Risperidone trials

	Mean	SD
Age, years	7.98	2.70
	<i>N</i>	%
Gender		
Male	174	84.5%
Female	32	15.5%
Race and Ethnicity		
White	149	72.3%
Black	16	7.8%
Hispanic	25	12.1%
Asian/Pacific Islander	9	4.4%
Other	7	3.4%
Educational Placement		
Regular education	47	22.8%
Regular education, some special education services	72	35.0%
Special education school	62	30.1%
Home school	9	4.4%
No school	14	6.8%
IQ ^a		
<70	110	53.4%
70	84	40.8%
ASD Diagnosis		
Autistic Disorder	163	79.1%
Asperger's Disorder	8	3.9%
PDD-NOS	35	17.0%
CGI-S		
4(moderate)	51	24.8%
5(marked)	99	48.1%
6(severe)	54	26.2%
7(extreme)	2	1.0%
	<i>M</i>	<i>SD</i>
ABC ^b		
Irritability	27.82	7.16
Social Withdrawal	16.36	8.69
Stereotypy	9.22	5.15
Hyperactivity	34.29	8.88

	Mean	SD
Inappropriate Speech	5.93	3.75
Vineland		
Communication	51.93	20.29
Daily Living Skills	43.19	19.79
Socialization	53.48	15.21
ADI-R		
Social Interaction	22.57	6.15
Communication Verbal ^c	15.63	5.43
Communication Non-verbal ^d	11.88	2.61
Stereotypy	6.63	2.78
CYBOCS-PDD		
Total Score	15.22	3.16
CASI		
PDD	23.04	7.14
Anxiety	15.40	9.58

* Missing data on baseline Target Problem in 19 subjects;

^a Missing IQ data for 12 subjects;

^b Higher scores indicate greater behavioral problems;

^c Missing communication verbal data for 54 subjects due to scoring conventions;

^d Missing communication non-verbal data for 90 subjects due to scoring conventions;

CGI-S = Clinical Global Impression-Severity; ABC = Aberrant Behavior Checklist; Vineland = Vineland Adaptive Behavior Scales; ADI-R = Autism Diagnostic Inventory-Revised; CYBOCS = Children's Yale-Brown Obsessive Compulsive Scale for Pervasive Developmental Disorders

Table 3

Demographic & Clinical Characteristics of 200^a Children with ASDs

Characteristic	Hot aggression only		Cold aggression only		Self-injury only		Self-injury and aggression		Non Aggression		χ^2	p value
	n	%	n	%	n	%	n	%	n	%		
Gender												
Male	55	84.6	25	78.1	26	78.8	15	88.2	47	88.7	2.60	0.63
Female	10	15.4	7	21.9	7	21.2	2	11.8	6	11.3		
IQ ^b												
<70	31	47.7	15	46.9	22	66.7	14	82.4	24	45.3	10.94	0.03*
70	28	43.1	15	46.9	10	30.3	2	11.8	27	50.9		
ASD diagnosis												
Autistic Disorder	54	83.1	23	71.9	27	81.8	16	94.1	37	69.8		
Asperger's Disorder	2	3.1	0	0	1	3.0	0	0	5	9.4	11.82	0.16
PDD-NOS	9	13.8	9	28.1	5	15.2	1	5.9	11	20.8		
	Mean	sd	mean	sd	mean	sd	mean	sd	mean	sd	F value ^c	p value
Age (yrs, mo)	7.29	2.27	7.72	2.61	8.11	3.25	8.89	3.39	8.61	2.49	2.42	0.05
Vineland												
Communication	54.54	20.17	53.16	17.52	47.42	17.81	38.53	15.46	55.66	22.59	1.11	0.36
Daily Living Skills	45.85	20.58	41.88	15.46	42.45	21.41	33.59	16.61	44.74	21.11	0.87	0.48
Socialization	55.69	13.82	54.47	12.26	52.70	16.39	41.59	16.72	55.68	15.80	1.83	0.13
ABC												
Irritability	27.98	6.89	27.38	7.94	29.70	5.54	33.00	7.91	25.38	7.01	5.11	<0.01**
Social Withdrawal	15.25	8.96	15.47	8.43	18.39	8.52	17.35	9.95	16.74	8.52	0.67	0.61
Stereotypy	8.81	5.33	9.59	5.46	8.61	4.64	12.24	4.70	9.11	5.25	1.18	0.32
Hyperactivity	34.76	8.18	34.75	8.51	32.52	9.20	35.41	9.18	34.09	10.10	0.48	0.75
Inappropriate Speech	6.33	3.81	5.85	3.61	5.39	3.99	5.18	3.84	6.02	3.65	0.77	0.55
CYBOCS-PDD												
Total score	15.45	2.96	14.50	2.70	15.21	3.24	14.53	4.24	15.45	3.33	0.73	0.57
CASI												
Anxiety scale	15.91	10.97	15.45	9.60	15.05	8.82	12.78	7.02	15.83	9.11	0.07	0.99
PDD-scale	22.84	6.85	22.81	6.92	22.71	7.30	27.06	5.84	22.37	7.72	0.82	0.52
Cardiovascular indices												
Heart rate (bpm)	100.20	13.94	102.00	14.81	96.80	14.79	103.35	27.65	96.79	17.55	0.82	0.52

Characteristic	Hot aggression only	Cold aggression only	Self-injury only	Self-injury and aggression	Non Aggression	
Blood pressure	107.29	13.88	106.81	13.07	108.04	15.07
				105.50	18.52	104.29
					11.41	0.34
						0.85

^a =6 participants with both hot and cold aggression were not included in analysis;

^b =Missing IQ data for 12 subjects

^c =ANCOVA analyses controlling for IQ (above and below 70). ANCOVA for age did not covary for IQ

* $p<0.05$;

** $p<0.01$

Table 4

Rate of Positive and Negative Response on CGI-I for Risperidone-treated Subjects in RUPP Trials by Aggression Subtype^a

Group	Positive Response on CGI-I ^b N (%)	Negative Response on CGI-I ^c N (%)	Chi square (compared to non aggression group)	p value
Non-aggression	33	20	-----	
Hot Aggression	45	20	0.63	0.43
Cold Aggression	22	10	0.37	0.54
SIB	20	13	0.02	0.88
Any aggression + any SIB	10	7	0.06	0.80
Hot Aggression and Hot SIB ^d	73	36	0.35	0.55

^a =does not include placebo group;

^b (positive response) = Much Improved or Very Much Improved;

^c (negative response) = all other CGI-I ratings;

^d = Hot Aggression, Hot SIB only and Hot SIB + aggression (any type);