Autistic-Spectrum Disorders in Down Syndrome: Further Delineation and Distinction from Other Behavioral Abnormalities

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The present study extends our previous work characterizing the behavioral features of autistic-spectrum disorder (ASD) in Down syndrome (DS) using the Aberrant Behavior Checklist (ABC) and Autism Behavior Checklist (AutBehav). We examined which specific behaviors distinguished the behavioral phenotype of DS + ASD from other aberrant behavior disorders in DS, by determining the relative contribution of ABC and AutBehav subscales and items to the diagnosis of ASD. A total of 127 subjects (aged 2–24 years; mean age: 8.4 years; ~70% male), comprising a cohort of 64 children and adolescents with DS and co-morbid ASD (DS + ASD), 19 with DS and stereotypic movement disorder (DS + SMD), 18 with DS and disruptive behaviors (DS + DB), and 26 with DS and no co-morbid behavior disorders (DS + none) were examined using the aforementioned measures of aberrant behavior. We found that subjects with DS + ASD showed the most severe aberrant behavior, especially stereotypy compared to DS + none and lethargy/social withdrawal and relating problems compared to DS + SMD. Specifically, relatively simple stereotypic behavior differentiated DS + ASD from DS + DB, whereas odd/bizarre stereotypic and anxious behavior characterized DS + ASD relative to DS + SMD and DS + none. Additionally, in a subset of subjects with DS + ASD and anxiety, social withdrawal was particularly pronounced. Overall, our findings indicate that a diagnosis of DS + ASD represents a distinctive set of aberrant behaviors marked by characteristic odd/bizarre stereotypic behavior, anxiety, and social withdrawal. © 2006 Wiley-Liss, Inc.

KEY WORDS: pervasive developmental disorder; stereotypic movements; childhood disintegrative disorder; anxiety; aberrant behavior checklist; autism behavior checklist; dual diagnosis; trisomy 21


INTRODUCTION

Down syndrome (DS) is the most common cause of genetically based mental retardation, occurring in an estimated 1 in 1000 live births [Moser, 1985]. Complex cognitive and neurobehavioral disorders can occur in association with DS, contributing to the within-syndrome variability often seen in neurogenetic disorders [Hodapp and Dykens, 2001]. There is, however, limited information available regarding the neurobehavioral phenotype of children with DS and co-morbid ASD or other neurobehavioral disorders, which have only recently begun to be delineated in a systematic manner [Clark and Wilson, 2003; Capone et al., 2005]. In an earlier study [Capone et al., 2005] we used the Aberrant Behavior Checklist (ABC) [Aman et al., 1985a] to identify patterns of problem behavior, which differentiated DS subjects with ASD from those with either Stereotypic Movement Disorder (DS + SMD), or those without serious behavioral problems (DS + none or typical DS). Compared to other DS subjects, those with ASD had substantially higher scores on the ABC, particularly with respect to stereotypy and social withdrawal. Demographic variables such as gender and age were only minor contributors to this characteristic profile. Furthermore, we demonstrated that aberrant behavior and cognitive function manifested inversely along a spectrum of severity within the diagnostic subgroups of ASD (namely, autism, pervasive developmental disorder, and childhood disintegrative disorder). These findings support the notion that ASD, SMD, and possibly other atypical behavior conditions represent distinct neurobehavioral phenotypes within DS, which can be distinguished from each other by means of their specific profile of cognitive-behavioral dysfunction.

The present study aims to expand our characterization of DS + ASD by introducing a second behavior-rating...
instrument, the Autism Behavior Checklist (AutBehav) [Krug et al., 1980], and by examining through items the specific behaviors that constitute the high degree of stereotypy and lethargy/social withdrawal associated with DS + ASD. Moreover, we distinguish DS + ASD from other abnormal behavior syndromes, namely DS + SMD and disruptive behaviors (DS + DB). A description of the specific problem behaviors associated with DS + ASD holds significance for planning and measuring the efficacy of therapeutic interventions, as well as characterizing the neurobiological bases of ASD in subjects with DS, which may be distinct from ASD associated with other genetically based disorders such as Fragile X syndrome [Kates et al., 2002; Kaufmann et al., 2003]. The overall goals of this study are therefore:

1. to generally describe the DS + ASD, DS + SMD, DS + DB, and DS + none groups in terms of overall severity of problem behavior.
2. to further characterize the types of behavior present in DS + ASD and differentiate them from DS + SMD and DS + DB using the ABC and AutBehav.
3. based on these types of behavior, to identify the specific problem behaviors, within the groups identified under the first goal, that contribute to the diagnosis of ASD by item analyses of the ABC and AutBehav.
4. to further examine the significance of specific behaviors identified in the third goal.

SUBJECTS

Population

The present study investigated cognitive and behavioral data from 127 subjects with DS. Of these, 64 subjects had co-morbid Autism Spectrum disorders (DS + ASD), 19 had co-existing stereotypic movement disorder (DS + SMD), 18 exhibited co-existing disruptive behaviors (DS + DB), and 26 had no major co-existing psychiatric condition (DS + none). These subjects were selected on the basis of completeness of data from an original cohort of 471 subjects, all of whom were recruited from the Down Syndrome Clinic at the Kennedy Krieger Institute between 1991 and 2001 (Table I). In all cases, DS was confirmed by a review of the karyotype report. The vast majority of subjects (~97% overall) had trisomy 21, the remainder were found to have complete unbalanced translocation of chromosome 21.

Definitions

Cases of ASD, SMD, and DB were identified according to DSM-IV criteria [APA, 1994]. Subjects with DS + ASD were defined as children who met diagnostic criteria for autism, pervasive developmental disorder—not otherwise specified (PDD), or childhood disintegrative disorder (CDD); subjects with stereotypic movement disorder (SMD) met criteria for this condition as described previously [Capone et al., 2005]. Subjects with DS + DB met criteria for either oppositional defiant disorder (ODD) or disruptive behavior disorder—not otherwise specified (DBD-NOS), but did not meet diagnostic criteria for autism, PDD, CDD, or SMD. DB was operationally defined as clinically significant (functionally impairing) behaviors corresponding to ODD or DBD-NOS with or without ADHD. Subjects with “typical” DS did not manifest significant behavioral aberration as determined by both parents and the examining physician. Children whose behavioral condition was better explained by a primary diagnosis of depression, obsessive-compulsive disorder, or tic disorder were excluded from the present study.

Consent

Approval for this study was granted by the Joint Committee on Clinical Investigation of the Johns Hopkins Medical Institutions. Written informed consent was obtained from the parents or legal guardians of all participating subjects. Verbal assent for cognitive testing was obtained from subjects whenever they were capable of understanding verbal explanation.

METHODS

DSM-IV Criteria

Subjects were categorized by clinical diagnosis according to DSM-IV criteria [APA, 1994] using all data obtained from behavioral assessments, including behavior questionnaires, semi-structured neurodevelopmental evaluation, and observation during unstructured play or social settings. A single evaluator (gtc) was responsible for rating subjects using DSM-IV criteria. Prior to 1994, the DSM-IIIR [APA, 1987] was used as the primary categorizing instrument, and these earlier evaluations were easily adapted into DSM-IV format, given the content overlap between the two versions.

Cognitive Testing

In order to assess the level of cognitive function in subjects with DS, either the Bayley Scales of Infant Development—Mental Scales (BSID) [Bayley, 1993] or the Stanford Binet Intelligence Scale, Fourth Edition (SB-IV) [Thorndike et al., 1986] was administered. The BSID was administered by clinical psychologists to children whose abilities fell below the 2-year level (N = 41). This test is standardized for children between 1 and 30 months of age and yields a mental age score, which was then used to compute a developmental quotient (DQ). Several subjects (N = 44) were tested by a neurodevelopmental pediatrician using the clinical adaptive test/case linguistic impairment auditory milestone scale (CAT/CLAMS), which has shown positive correlation with BSID scores in children with cognitive impairment [Hoon et al., 1993]. Subjects whose mental age on the BSID exceeded 2 years and who were able to establish a true basal (N = 53) were administered with SB-IV. This scale integrates 15 subtest scores across 4 domains (verbal reasoning, abstract/visual reasoning, quantitative reasoning, and short-term memory), which in composite are used to calculate a scaled score (IQ). A total of 10 subjects did not receive cognitive testing and were not included in any analyses for the present study. Not all subjects who received cognitive testing were used in final analyses due to incompleteness of other data. For data analysis purposes, both the BSID-derived DQ and the SB-IV scaled score were labeled as “IQ,” and references to IQ in this text refer to both IQ and IQ-equivalent measures.

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*Due to incomplete IQ data, only 52 DS + ASD subjects were available for analyses.

**Significantly different (P < 0.05) compared to DS + none, or to DS + Autism within the DS + ASD group.**
Aberrant Behavior Checklist

The ABC [Aman et al., 1985a] is a 58-item, parent-report measure which measures severity of behaviors continuously in five subscales: Irritability, lethargy/social withdrawal, stereotypy, hyperactivity, and inappropriate speech. Items are scored from 0 (not problematic) to 3 (severely problematic). The ABC was originally designed for use in institutionalized populations, but subsequently was successfully applied to a population with DS [Aman et al., 1986b]. Rojahn and Helsel [1991] successfully applied this test to children with dual diagnosis. Per checklist instructions, parents were asked to rate each of the 58 behaviors in their child during the past month. For the purpose of further analysis of specific behaviors, and on the basis of our clinical experience (rmg, ccc), we determined whether each item of the lethargy/social withdrawal subscale represented a behavior better labeled as social indifference or social withdrawal [Budimirovic et al., 2006]. We concluded that the majority of items (12 of 16) corresponded to social indifference, with two items classified as social withdrawal, and the remaining two associated with both (tending toward social withdrawal). Although this item classification has not yet been validated, this approach aided in the analysis and interpretation of behavioral data.

Autism Behavior Checklist

The AutBehav [Krug et al., 1980] is a 57-item, parent-report screening instrument which records categorically the presence or absence of autism-associated behaviors in five subscales: sensory, relating, body and object use, language, and social and self help. Each item is pre-weighted (1–4) in one of these five subscales. Higher scores indicate greater severity or frequency of problem behavior. The AutBehav is widely used for screening and diagnostic purposes, though its applicability in differentiating ASD from other developmental disorders has been reported to be somewhat limited [Rellini et al., 2004]. In a manner similar to our classification of ABC lethargy/social withdrawal items, we coded AutBehav relating items as social indifference, social withdrawal (or both), or anxiety. According to this classification, six items corresponded to social indifference, three to social withdrawal, two to both, and one to anxiety.

Data Analysis

Descriptive statistics were used to determine the relative distribution of values and aided in the interpretation of our main statistical approach, namely regression models with ASD diagnosis as the outcome variable. We conducted analyses of variance and covariance (ANOVAs and ANCOVAs, respectively) to examine differences in scores (IQ, ABC, AutBehav) between groups and to determine (by F-test) the degree to which these scores differentiated from each group. Since our initial analyses indicated significant between-group differences with respect to IQ (Table I), we included IQ as a covariate in every behavioral analysis. We also included age as a co-variate to account for the fact that subjects were not directly matched by age and applied post hoc analyses such as Scheffe’s test [Scheffe, 1953] to minimize the effects of variance heterogeneity, non-Gaussian distribution, and unequal N values.

We employed multivariate and ordered logistic regression models to examine the relative contributions of behavior subscale scores (the five subscales of the ABC or AutBehav) to total ABC and AutBehav scores and likelihood of ASD diagnosis, respectively. As before, age and IQ were included as co-variates in these models. Similar models were used to study the contributions of ABC item scores to subscale scores and likelihood of ASD diagnosis. From our logistic models, we used the P- and Chi-square values corresponding to logistic likelihood ratio tests to determine the relative contribution of each variable. These tests assess the deviance of a fitted model including each variable against a model not including each variable, and were in general agreement with P- and Chi-square values obtained from the Wald test. We also derived log odds ratios describing the increasing probability of ASD diagnosis per unit increase in subscale or item score.

Our analyses were conducted in a hierarchical fashion, examining first overall differences in severity of problem behavior (comparing ABC and AutBehav total scores), then differences in behavioral subscales, and finally differences in individual behaviors (item scores). When significant differences or contributors in a more general level were found, we conducted analyses in the next more specific level, and so on.

RESULTS

Cohort Characteristics

Our sample included a predominance of males, especially in the DS + ASD, DS + SMD, and DS + DB groups (Table I). As the subjects in our sample are representative of the referral pattern to the DS clinic, it is likely that this overrepresentation of males is not the result of mere sample bias. No significant differences in age between groups were found, nor were males and females significantly different with respect to age, IQ, or ABC, and AutBehav scores.

Overall Cognitive Function

The DS + ASD group was found to have significantly lower IQ/IQ-equivalent scores than subjects with typical DS (Table I). Within the DS + ASD group, subjects with autism showed the lowest IQ scores, though they were not significantly different from the CDD group in this regard (Table I). Because of this similarity, and because the CDD group was otherwise behaviorally indistinct from the autism group, subjects with CDD were excluded from between-group analyses and were only used in intra-ASD comparisons. This practice, though it has been questioned, is not uncommon, given the reported difficulty differentiating CDD from autism as a distinct diagnosis [Hendry, 2000].

Differences Between Diagnostic Groups

DS + ASD within group comparisons. Intra-ASD comparisons revealed that subjects with autism and CDD displayed similarly severe problem behavior, as measured by both the ABC and AutBehav, followed by the PDD group, which achieved significantly lower scores than autism or CDD on the AutBehav (P < 0.01; Table II). Mean ABC inappropriate speech scores were significantly higher in the PDD group than in autism or CDD (Table III), and the mean scores for AutBehav sensory and relating were significantly lower for the PDD

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*Not including CDD group, as discussed in text.

**Significantly different (P < 0.05) compared to DS + none, or to DS + Autism within the DS + ASD group.
group when compared to the other two ASD subgroups [Table IV]. Using both scales, the autism and CDD groups were relatively indistinct from each other in terms of mean scores.

**IV)Q1. Using both scales, the autism and CDD groups were aNot including CDD group, as discussed in text.**

- DS + ASD and DS + none group comparison. The DS + ASD group had higher total scores than any other group on both the ABC and AutBehav (Table II). When the DS + ASD and DS + none groups were compared, we found that scores in each subscale of both the ABC and AutBehav were significantly higher (P < 0.01) in the group with DS + ASD, thus, we examined the F-statistic associated with each ABC or AutBehav subscale. ABC stereotypy was the strongest differentiating factor between DS + ASD and DS + none (Table III). Similarly, subjects with DS + SMD showed higher scores than DS + none in every subscale of the AutBehav, especially the body and objects use and sensory subscale (Table IV).

 Nonetheless, in these groups, our logistic models showed ABC stereotypy to be the only significant contributor to the diagnosis of ASD (Fig. 1), with an associated log odds 2.083 (not shown). Our logistic models showed no clear predominance of any AutBehav subscale in the group comprising subjects with DS + ASD and typical DS, as no subscale reached significance.

**DS + ASD and DS + SMD group comparisons.** Comparatively analyses of covariance between the DS + ASD and DS + SMD groups again revealed that ABC stereotypy was the strongest differentiating factor between DS + ASD and DS + SMD and was associated with higher scores in DS + ASD (Table III). Similarly, subjects with DS + SMD showed higher scores than DS + none in every subscale of the AutBehav, especially the body and objects use and sensory subscales (Table IV).

Logistic models used in the combined DS + ASD/DS + SMD cohort showed ABC lethargy/social withdrawal to be the only subscale which predicted ASD (Fig. 2). The odds ratios for ABC lethargy/social withdrawal were slightly greater than one. With respect to the AutBehav, relating was found to have the greatest impact on ASD diagnosis, with associated odds ratios of approximately one.

**DS + ASD and DS + DB group comparison.** Comparatively analyses of covariance between the DS + ASD and

![Fig. 1. Logistic regression model for the ABC in the DS + ASD/DS + none cohort.](image-url1)

![Fig. 2. Logistic regression model for the ABC in the DS + ASD/DS + SMD cohort. Lethargy/social withdrawal is the only significant contributor to ASD diagnosis in this cohort. Only item #30 contributed significantly to the diagnosis of ASD, whereas #3 contributed at trend-level after Benferroni correction for the predominance of social indifference items (altered significance threshold = 0.05/16/3 = 0.001).](image-url2)
DS + DB groups revealed that ABC hyperactivity and ABC irritability scores were higher in DS + DB. Notably, both of these subscales were higher in the DS + DB group than in any other group, including the otherwise more affected DS + ASD group (Table III). Compared to subjects with typical DS, those with DS + DB also showed particularly high AutBehav sensory and social and self help scores (Table IV). Studying the differential contribution of each ABC subscale to ASD diagnosis in these groups, we found stereotypy to be predictive of ASD (Fig. 3). The relative effect of this subscale using odds ratios was roughly equal to one. On the AutBehav subscales, we found only a trend-level influence of body and object use to ASD diagnosis.

Overall, comparing the subscales which most strongly predicted the diagnosis of ASD in the combined groups, we found that overall, AutBehav relating was the most significant contributor to ASD in both the DS + ASD/DS + none and DS + ASD/DS + SMD combined groups.

**Differentiation by Specific Behaviors**

Having determined by logistic regression analyses which subscales (i.e., ABC stereotypy, lethargy/social withdrawal, and AutBehav relating) generally/categorically differentiated each group, we then focused on the individual items from these subscales in an effort to identify the specific behaviors responsible for the overall aberrant behavior profiles we observed.

**Stereotypy differentiates DS + ASD from DS + none and DS + DB.** Ordered logistic models of ABC items revealed that item #17 (odd, bizarre behavior) of ABC stereotypy contributed most significantly to the occurrence of ASD compared to DS + none (Fig. 1). Items #11 (stereotyped, repetitive movements) and #27 (moves or rolls head back and forth) also differentiated DS + ASD (from DS + none). DS + ASD was best differentiated from DS + DB by ABC stereotypy item #11 (stereotyped, repetitive movements; Fig. 3).

**Social withdrawal differentiates DS + ASD from DS + SMD.** When examining items from ABC lethargy/social withdrawal in DS + ASD and DS + SMD, item #30 (isolates self from others) emerged as the most significant contributor to ASD in this subscale. When differentiating DS + ASD from DS + none, ABC stereotypy item #17 (odd, bizarre behavior) was best differentiated from DS + none. AutBehav relating was the strongest item in this respect. When differentiating DS + ASD from DS + SMD, AutBehav relating #43 (often frightened or very anxious) was the strongest item. In order to examine any potential differences between subjects with and without anxious behavior, we split the DS + ASD group into anxious and non-anxious subgroups. We found no significant differences in age or IQ, although the group with anxiety had slightly higher average IQ scores (p = 0.1155). With respect to ABC and AutBehav scores, while we observed no statistically significant differences (possibly due to insufficient statistical power resulting from small sample size), one notable trend emerged. Of the lethargy/social withdrawal items, only #30 (isolates self from others), related to social withdrawal, was higher in subjects with anxious behavior, whereas those items relating to social indifference were lower in subjects with anxious behavior (Fig. 4).

**ASD Status and Social Indifference/Withdrawal**

Using an analytical approach whereby we determined whether each item of ABC lethargy/social withdrawal and AutBehav relating represented a behavior better labeled as social indifference or social withdrawal, along with the results of our logistic regression models, we found that DS + ASD was differentiated from DS + SMD primarily by more pronounced social withdrawal behavior (#30—isolates self from others), although one behavior corresponding to social indifference (#3—listless, sluggish, inactive) was a trend-level contributor to this differentiation. The significance of the social indifference versus withdrawal differences was determined using a modified Bonferroni correction strategy, whereby social indifference items were subjected to an additional divisor of three to reflect the fact that they were three times more prevalent than social withdrawal items in our classification of the ABC lethargy/social withdrawal subscale.

Comparing the most significant items from ABC stereotypy, lethargy/social withdrawal and AutBehav relating against each other, we found that, when differentiating DS + ASD from DS + none, ABC stereotypy item #17 (odd, bizarre behavior) was the strongest item in this respect. When differentiating DS + ASD from DS + SMD, AutBehav relating #43 (often frightened or very anxious) was the strongest item. In order to examine any potential differences between subjects with and without anxious behavior, we split the DS + ASD group (as this was the predominant group in which anxious behavior was reported) into anxious and non-anxious subgroups. We found no significant differences in age or IQ, although the group with anxiety had slightly higher average IQ scores (p = 0.1155). With respect to ABC and AutBehav scores, while we observed no statistically significant differences (possibly due to insufficient statistical power resulting from small sample size), one notable trend emerged. Of the lethargy/social withdrawal items, only #30 (isolates self from others), related to social withdrawal, was higher in subjects with anxious behavior, whereas those items relating to social indifference were lower in subjects with anxious behavior (Fig. 4).

**DISCUSSION**

In this study we analyzed aberrant behaviors measured by the ABC and AutBehav in order to characterize the neurobehavioral phenotype of DS + ASD and to differentiate it from other aberrant behavior disorders in DS. Our findings indicate that ASD manifests as a distinct behavioral phenomenon in DS and can be differentiated from typical DS by anxious behavior and complex and unusual stereotypy, from DS + SMD by social withdrawal and anxious behaviors, and from DS + DB by relatively simple stereotypic behavior. Moreover, this method demonstrates the efficacy of examining ABC and AutBehav items as individual aberrant behaviors in addition to overall classes of problem behavior when delineating...
behavior syndromes in DS and, perhaps, in other developmental disorders. This approach, to the best of our knowledge, has not been attempted to date.

In DS, there appears to be a disconnection between severity of aberrant behavior and severity of cognitive dysfunction generally. Although our finding that DS + ASD is associated with significantly higher total ABC and AutBehav scores corresponds to our and other earlier reports of a link between low-cognitive function and severity of autistic-like behaviors [Bartak and Rutter, 1976; Capone et al., 2005] it is nonetheless important to note that the DS + DB group, which had IQ scores comparable to the DS + none group, scored higher on every subscale of the ABC and AutBehav than the DS + none group, and showed higher scores than DS + ASD on ABC irritability and hyperactivity. This suggests that the neural processes underlying these behaviors (hyperactivity, impulsivity, disruptiveness, and aggression) in DS are largely distinct from those affecting primarily cognitive function, and further emphasizes the importance of examining specific, in addition to general, behaviors in DS. Also, our finding that the autism, CDD, and PDD groups formed a continuum with respect to both global cognitive function and aberrant behavior. This approach, to the best of our knowledge, has not been attempted to date.

The present study also provides greater detail to our original characterization of lethargy/social withdrawal in DS + ASD. Although both DS + ASD and DS + SMD showed significantly more severe lethargy/social withdrawal than DS + none (Table III), self isolation (social withdrawal) in particular characterized DS + ASD (Fig. 2).

Examining the relationship between social withdrawal and anxious behavior in subjects with DS + ASD, we found that subjects with anxious behavior scored selectively higher on the social-withdrawal associated ABC lethargy/social withdrawal item #30 (isolates self from others), even though these same subjects had lower ABC total and lethargy/social withdrawal scores, and lower scores for social-indifference related items. Hence, social withdrawal and anxious behavior appear to be related in DS + ASD. It may be that anxiety plays an antecedent role to active social withdrawal in DS + ASD, as suggested by preliminary studies of this phenomenon in Fragile X syndrome with co-morbid ASD [Hagerman, 2002; Budimirovic et al., 2006]. Additional studies of social withdrawal and anxiety-related behaviors of DS + ASD will undoubtedly provide greater insight into these potentially related phenomena.

While it could be argued that most cognitive-behavioral domains vary continuously across the entire population of subjects with DS, we have been impressed by the apparent clustering of certain complex neurobehavioral traits in association with the level of cognitive function, in addition to a pronounced gender bias favoring males, which appears to be operating. This study advances efforts toward defining and characterizing neurobehavioral phenotypes associated with DS. The characteristic cognitive-behavioral profile of DS + ASD compared to DS + SMD or DS + DB as described in this study, suggests that these phenotypes are distinct from that observed in persons with DS without behavioral comorbidity. The variability of behavioral phenotype(s) associated with DS appears to be determined in part by neurobiological processes under the control of genes affected by or mapping to chromosome 21, which contains about 360 unique genes [Gardiner et al., 2003]. Thus, given the neurobehavioral variability seen in such single-gene disorders as Fragile X syndrome [Hagerman, 2002; Kau et al., 2004; Kaufmann et al., 2004], trisomy 21 is likely to result in an even wider spectrum of neurobehavioral phenotypes, as a consequence of complex neurobiological determinants. The further characterization of these phenotypes using detailed, yet readily identifiable behavior items, as was done in this study, may permit more accurate and effective diagnosis, intervention, and treatment despite phenotypic complexity.

The characterization of the DS + ASD phenotype in particular permits for a more precise elucidation of the neurobiology of autism using a combination of neuroimaging and molecular techniques. Understanding how abnormal neuronal circuitry influences the manifestation of specific behaviors can offer clues to the prevailing mechanisms of ASD in other genetic disorders such as Fragile X syndrome, which appear distinct from those affecting primarily cognitive function, independent of aberrant behavior in DS.
from those observed in DS + ASD [Kates et al., 2002; Kaufmann et al., 2003; Kau et al., 2004]. Finally, delineation of specific behavioral profiles is important for the proper design and implementation of therapeutic interventions for young children with DS [Capone, 2004]. Not only would identified children require a different package of intervention services, but those with bona-fide neurobehavioral co-morbidity could further benefit from astute pharmacological treatment designed to minimize interfering maladaptive behaviors.

ACKNOWLEDGMENTS

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REFERENCES


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