Timing of the Diagnosis of Autism in African American Children

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abstract

OBJECTIVES: African American (AA) children affected by autism spectrum disorder (ASD) experience delays in diagnosis and obstacles to service access, as well as a disproportionate burden of intellectual disability (ID) as documented in surveillance data recently published by the US Centers for Disease Control and Prevention. Our objective in this study was to analyze data from the largest-available repository of diagnostic and phenotypic information on AA children with ASD, and to explore the wide variation in outcome within the cohort as a function of sociodemographic risk and specific obstacles to service access for the purpose of informing a national approach to resolution of these disparities.

METHODS: Parents of 584 AA children with autism consecutively enrolled in the Autism Genetic Resource Exchange across 4 US data collection sites completed event history calendar interviews of the diagnostic odysseys for their children with ASD. These data were examined in relation to developmental outcomes of the children with autism and their unaffected siblings.

RESULTS: The average age of ASD diagnosis was 64.9 months (±49.6), on average 42.3 months (±45.1) after parents' first concerns about their children's development. The relationship between timing of diagnosis and ASD severity was complex, and ID comorbidity was not predicted in a straightforward manner by familial factors associated with cognitive variation in the general population.

CONCLUSIONS: These findings document significant opportunity to expedite diagnosis, the need to further understand causes of ID comorbidity, and the necessity to identify effective approaches to the resolution of disparities in severity-of-outcome for AA children with autism.

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Dr Constantino drafted the initial manuscript, conceptualized and designed the study, secured funding, assumed the role of principal investigator for data collection site, and coauthored the Diagnostic Odyssey data collection instrument; Ms Abbacchi drafted the initial manuscript, coordinated and supervised data collection, and conducted analyses of data; Drs Saulnier and Klaiman drafted the initial manuscript and coordinated and supervised data collection; Dr Mandell drafted the initial manuscript and coauthored the Diagnostic Odyssey data collection instrument; Ms Zhang coordinated and supervised data collection and conducted analyses of data; Ms Hawks Conducted analyses of data; Dr Bates coordinated and supervised data collection; (Continued)

WHAT'S KNOWN ON THIS SUBJECT: African American (AA) children with autism experience racial disparities in timing of diagnosis and access to quality interventions. AA children experience twice the rate of comorbid intellectual disability and higher rates of misdiagnosis of autism compared with non-Hispanic white children.

WHAT THIS STUDY ADDS: These data reveal a 3-year time lag between parental recognition of developmental delay and autism diagnosis among AAs, and that excess intellectual disability burden cannot be explained by ascertainment bias or by traditional familial predictors of cognitive outcome.

To cite: Constantino JN, Abbacchi AM, Saulnier C, et al. Timing of the Diagnosis of Autism in African American Children. *Pediatrics.* 2020;146(3):e20193629

Despite implementation of the US Centers for Disease Control and Prevention (CDC) "Learn the Signs, Act Early" campaign, recent community surveillance data[1] has revealed persistent delays in the timing of diagnosis of autism spectrum disorder (ASD). Overall, 39% of children with ASD did not have a comprehensive evaluation on record until after age 48 months, although 85% had parents' developmental concerns documented before age 36 months. Typically, the timing of diagnosis is earlier for more severe cases of ASD; during historical eras in which the rates of community diagnosis of autism were lower for minority children, those who were identified tended to exhibit more severe syndromes.[2]

According to 2018 US surveillance data, the racial gap in identification has now narrowed to a difference of just 1.2 per 1000 (16 per 1000 for African American [AA] vs 17.2 per 1000 for non-Hispanic white [NHW]).[1] Delays in diagnosis remain greater, on average, for AA children, and the consequences of these delays are particularly severe because of known disparities in the acquisition and quality of intervention services once a diagnosis has been made.[3–5] AA and Latino children with ASD, on average, are more likely to have carried non-ASD diagnoses before a definite ASD diagnosis, have poorer access to health care services, and are less likely to have a medical home.[4,6–8]

A particularly serious disparity is that the proportion of AA children with ASD and comorbid intellectual disability (ID) is double that of NHW children (44% vs 22%).[1] Historically, when community diagnostic rates for ASD were disproportionately low for minority children, it was assumed that higher rates of ID comorbidity among minority populations might be explainable on the basis of underidentification of higher-IQ cases in the community. Given what is now a near-equivalence of prevalence across race, this explanation is no longer tenable. Even if the residual prevalence gap were assumed to be composed exclusively of children without ID, it would result in an adjusted estimate of 41% of AA children with ASD having comorbid ID.

Therefore, we leveraged an ongoing data collection of AA children with ASD and their first-degree relatives (US National Institutes of Health [NIH] MH100027; to our knowledge, the most comprehensive data collection to inform these issues) to explore potential drivers of delay in diagnosis and the ID disparity. Specifically, we sought to identify targets for accelerating the timing of diagnosis in AA children with autism[9] and to determine if commonly observed family and social correlates of cognitive variation among minority youth in the United States predicted variation in IQ among AA children with ASD.

With the analyses presented in this report, we incorporated 4 elements of data acquisition. The first was an event history calendar interview on the pathway from earliest recognition of developmental delay to each child's diagnosis.[10] The second involved direct cognitive assessment of the children and their close relatives; this allowed a direct test of association of traditional correlates of low IQ with the cognitive outcomes of the children with ASD in this study, who manifested a wide and fully representative range of IQ for children with ASD. Third, as a direct validation of the CDC epidemiological surveillance statistics, and a check on the population-representativeness of the sample of AA children consecutively enrolled in this data collection, we seperately analyzed the subset of children who fell within the birth years and Missouri catchment area for the CDC surveillance program, incorporating data from the later. Fourth, because of the nature of the parent study, we were able to specify the genetic ancestry of the study population.

METHODS

Participants were enrolled in Autism Genetics Network, Phase II: Increasing the Representation of Human Diversity (US NIH MH100027; institutional review board 11-000397). The parents of all participants provided individual informed consent; the assent process was conducted with children, when deemed appropriate, in accordance with institutional review board guidelines. Data collection spanned the years 2013 to 2018.

Participants

The sample comprised 584 consecutively enrolled AA children with ASD (466 male, 118 female) and their family members at Washington University in St Louis, MO (N = 205); Emory University in Atlanta, GA (N = 181); University of California, Los Angeles (N = 131); and Albert Einstein College of Medicine in Bronx, NY (N = 67); see Sample Characteristics, Participants' State of Residency, and Study Enrollment in Supplemental Information for details of subject accrual.

At both the Washington University and Emory University sites, cognitive assessments were conducted on the first-degree relatives (biological parents and siblings) of all subjects for whom both parents were AA.

Genetic confirmation of ancestry of all subjects is presented in Genetic Confirmation of African Ancestry in Supplemental Information and Supplemental Fig 1.

Measures

A Diagnostic Odyssey Interview instrument, modeled on the Event History Calendar Interview method, was developed for the study and implemented with the primary caregiving parent of each subject to

characterize service-seeking experiences for AA and minority families and obstacles to ASD diagnosis, treatment, and medical care. A complete description is provided in Development of Event History Calendar Interview: Diagnostic Odyssey in Supplemental Information.

ASD Diagnosis and Characterization of Severity

A research-certified rater administered the Autism Diagnostic Observation Schedule (ADOS or ADOS-2) to each child. Parent-report information was collected by using the Vineland Adaptive Behavior Scales, Second Edition (Vineland-II), the Autism Diagnostic Interview-Revised (ADI-R; operationalized as retrospective reports of ASD severity) and/or a Diagnostic Statistical Manual IV– or 5–based diagnostic interview, Social Responsiveness Scale, and Social Communication Questionnaire (SCQ); details provided in ASD Clinical Severity and Verbal or Nonverbal Designation in Supplemental Information and Supplemental Table 6.

Cognitive Assessments

In conducting cognitive assessments on the subjects, we implemented a decision-tree to select the instrument, based on clinical convention and accounting for each individual's level of behavioral adaptation and age (see Description of Cognitive Assessments, Calculation of Proxy-IQ for Participants With ASD, and Cognitive Assessment of Undiagnosed First-Degree Relatives in Supplemental Information; Supplemental Tables 7 and 8; Supplemental Fig 2). In Missouri, we confirmed ID (IQ $\leq$ 70) among those who had been identified in the Missouri CDC surveillance program and carried a co-occurring Autism and Developmental Disabilities Monitoring (ADDM) Network case designation of ID (see Overlap of the Missouri Sample With 8-Year-Olds Ascertained From the US CDC ADDM Program in Supplemental Information, Supplemental Table 9).

Statistical Analysis

After computation of descriptive statistics, we compared parent-reported delays in diagnosis and services in specific subgroups of patients, defined by indices of clinical severity, IQ, and acquisition of verbal language. Bivariate correlations were computed to quantify associations between the timing of first concerns, diagnosis, and initiation of services with clinical severity and IQ.

Finally, we used hierarchical regression to estimate the proportion of variance in adaptive and cognitive function that was accounted for by income, gender, and estimated gestational age at birth (model 1), retrospective reports of ASD severity (model 2), age of ASD diagnosis (model 3), and presence versus absence of early gross motor delay (model 4); see Hierarchical Regression Analysis in Supplemental Information for an expanded description.

RESULTS

Comparison of the Research Sample With Reported US CDC Surveillance Data

In Table 1, we depict the characteristics of our AA research sample in relation to data reported in 2018 from the US CDC Surveillance Program.[1] The median age of diagnosis in our sample was 48 months, and the mean age of diagnosis was 64.9 months. The proportion of subjects in our sample with documented ID (by direct, in-laboratory psychometric assessment) was 35.2%. Among eight CDC-identified children recruited into the current study, seven were confirmed intellectually disabled by direct assessment; one, however, was found to have a nonverbal IQ of 90.

Nature of Delays in the Timing of Diagnosis

We summarize in Table 2 the nature of delays in diagnosis as a function of key demographic characteristics, segregated by level of functioning of the subjects. The mean age of diagnosis (64.9 months) came, on average, >3 years after parents reported having initial concerns about their child's language, behavior, or development (mean = 23.0 months $\pm$ 17.9). In this sample, 98.2% of the families reported having some type of insurance coverage at the time of first concerns (49.3% private, 45.8% public, and 4.7% other). There was considerable variation across the recruitment sites, with diagnostic delays ranging from an average of 32 months (Los Angeles) to 53 months (St Louis), and proportion of subjects with ID ranging from 12.5% (New York) to 49.1% (Atlanta, where median household income and level of parental education of enrolled subjects was highest). Age at diagnosis ranged from an average of 54 months at the New York site to 80 months at the St Louis site. Subjects with comorbid ID tended to

TABLE 1 Research Sample Characteristics in Relation to US CDC Surveillance Data Reported in Baio et al[1]

	All Study Sites *N* = 584 (517 families)	US CDC AA	US CDC NHW	US CDC All Races
Age at study enrollment[a]	9.6 y	8 y	8 y	8 y
Sex ratio	3.9	NA	NA	4.0
Median age of diagnosis, mo	48[b]	NA	NA	52
Proportion with ID, %	35.2	44.0	22.0	31.0

NA, not available within the CDC report.

[a] Age of ascertainment for US CDC surveillance data occurs during the calendar year that the child turns 8 y.

[b] Mean age of ASD diagnosis for all sites is 64.9 $\pm$ 49.6; see Table 2 for additional information.

TABLE 2 Delays in Diagnosis, as a Function of Selected Demographic Characteristics

	WUSTL *N* = 205 (179 families)	Emory *N* = 181 (165 families)	UCLA *N* = 131 (108 families)	Einstein *N* = 67 (65 families)	All Sites *N* = 584 (517 families)	Cross Site Comparison ANOVA, *P*	Mean ADI-R Social (Verbal Subjects)[a]	Mean ADI-R RRB (Verbal Subjects)[b]	IQ Association[c]	Verbal Versus Nonverbal Subjects *t* tests[d]
Age in months at study enrollment, mean (SD)	127.0 (62.4)	93.1 (48.4)	131.0 (62.0)	113.8 (49.7)	115.9 (59.0)	<.001	—	—	—	—
Age in months at parental first concerns, mean (SD)	26.7 (23.0)	20.3 (12.5)	22.3 (14.8)	19.1 (12.7)	23.0 (17.9)	<.001	−0.09	−0.18**	0.08	Verbal = 24 m; nonverbal = 17 m; *P* <.001
Age in months parent first shared concerns with a professional, mean (SD)	36.9 (29.6)	23.8 (17.2)	26.8 (16.3)	23.2 (17.6)	29.1 (23.1)	<.001	−0.05	−0.09	0.16**	Verbal = 31 m; nonverbal = 20 m; *P* <.001
Age in months at initiation of services, mean (SD)	49.9 (30.4)	36.5 (24.0)	41.3 (20.7)	35.5 (32.6)	42.3 (27.5)	<.001	−0.00	−0.10	.14**	Verbal = 45 m; nonverbal = 29 m; *P* <.001
Age in months child received ASD diagnosis mean (SD)	80.0 (58.1)	57.9 (37.4)	55.6 (43.7)	54.3 (48.5)	64.9 (49.6)	<.001	−0.09	−0.18**	0.16**	Verbal = 71 m; nonverbal = 36 m; *P* <.001
Delay in diagnosis, months, mean (SD)	53.0 (54.1)	38.1 (35.2)	31.8 (37.0)	35.0 (41.5)	42.3 (45.1)	<.001	−0.06	−0.12*	0.14**	Verbal = 47 m; nonverbal = 20 m; *P* <.001
Median household income at time of first concerns	$28 000	$50 000	$36 000	$45 000	$37 000	<.001	−0.04	0.12	0.06	*P* <.99
Parental level of education: college degree	25.1%	43.2%	21.5%	31.3%	30.2%	<.001	−0.14*	0.05	.10*	*P* <.93
Proportion of subjects with ID[e]	29.4%	49.1%	36.7%	12.5%	35.2%	<.001	—	—	—	—

RRB, restricted and repetitive behavior; WUSTL, Washington University in St. Louis; —, not applicable.

[a] Mean ADI-R social domain scores; Pearson correlation coefficient.

[b] Mean ADI-R restricted and repetitive behavior domain scores; Pearson correlation coefficient.

[c] Participants with ASD IQ-Proxy score; Pearson correlation coefficient.

[d] Comparison of means for verbal versus nonverbal subjects as a function of delay in diagnosis variables.

[e] For a more detailed analysis of cognitive scores across sites and by measure, refer to Supplemental Table 7.

* Indicates *P* value significant at .05 level (2-tailed). ** Indicates *P* value significant at .01 level (2-tailed).

be diagnosed earlier than those without ID ($P < .001$). Note that for all sites, the average age of initiation of service use was 1 to 3 years earlier than ASD diagnosis, suggesting that the services delivered were unlikely to have been specific for autism.

Data on the timing of milestones in the diagnostic process across the 4 sites is summarized in Table 3. Across all sites, 35.6% of families reported experiencing significant wait times to see a professional, and 41.6% reported seeing multiple professionals before receiving the ASD diagnosis. Fourteen percent reported seeing ≥6 professionals before being diagnosed with ASD, and 31.3% cited that a lack of available professionals contributed to delays in diagnosis.

Correlates of IQ

Children with ASD and their first-degree relatives exhibited a very broad IQ distribution (see Supplemental Figs 2 and 3, Supplemental Tables 7 and 8). We note that the mean IQ scores of the children who were testable (78.9 ± 21.7) were commensurate with (and somewhat higher than) their mean standardized scores for adaptive functioning on the Vineland-II (68.4 ± 11.5). We observed a relative absence of association between the IQ scores of children with ASD and those of their first-degree relatives (parents: $P = .27$; nondiagnosed siblings: $P = .60$). This is reflected in bivariate correlations presented in Table 4 and in an analysis of variance considering categories of cognitive impairment among the children with ASD ($P = .77$; see Stratification of the Sample Based on IQ-Proxy Scores of Participants With ASD in

TABLE 3 Milestones in the Diagnostic Process Derived From Diagnostic Odyssey Interview Data by Parent-Report

	WUSTL (N = 191), %	Emory (N = 140), %	UCLA (N = 121), %	Einstein (N = 65), %	All Sites (N = 517), %	Across Site Comparison χ^2	Mean ADI-R Social (Verbal Subjects)[a]	Mean ADI-R RRB (Verbal Subjects)[b]	Verbal v. Nonverbal Subjects χ^{2c}
Required 3–5 visits to professionals	27.7	27.9	23.0	31.3	27.1	NS	NS	NS	NS
Required ≥6 visits to professionals	22.5	12.1	5.7	12.5	14.5	$P < .001$	NS	NS	NS
Experienced a significant wait time to see a professional	36.6	42.1	30.6	27.7	35.6	NS	NS	NS	NS
Costs associated with the evaluation and diagnostic process	11.5	20.0	4.1	7.7	11.6	$P < .001$	NS	1; $P < .04$	Nonverbal = 4.4%; verbal = 13.6%; $P < .01$
Lack of available places or professionals to receive an evaluation in their area	28.3	45.7	21.5	27.7	31.3	$P < .001$	NS	0.7; $P < .02$	NS
Poor quality of the evaluation(s)	12.6	10.0	8.3	15.4	11.2	NS	NS	NS	NS
Scheduling conflicts between parent or caregiver and professionals	11.5	12.9	3.3	16.9	10.6	$P < .01$	NS	NS	NS
Difficulties due to lack of transportation to appointments	6.8	3.6	2.5	15.4	6.0	$P < .002$	2.3; $P < .05$	1.1; $P < .05$	NS
Difficulties with insurance coverage	11.5	16.4	4.1	9.2	10.8	$P < .02$	NS	NS	Nonverbal = 5.5%; verbal = 12.4%; $P < .06$

For all individuals enrolled in the study, 40.4% of the sample had received a diagnosis of another condition before receiving their ASD diagnosis, and 14.7% of the children received their first ASD diagnosis as part of the research evaluation itself (mean age of diagnosis = 118.8 ± 70.1). The most common misdiagnosis was global developmental delay (40.7%), followed by attention-deficit/hyperactivity disorder (38.9%), and speech and language delay (12.4%). NS, not significant; RRB, restricted and repetitive behavior; WUSTL, Washington University in St. Louis.

[a] Comparison of mean ADI-R social domain scores for subjects who endorsed experiencing specific barrier to care versus subjects who did not endorse barrier to care; t tests.

[b] Comparison of mean ADI-R RRB domain scores for subjects who endorsed experiencing specific barrier to care versus subjects who did not endorse barrier to care; t tests.

[c] Proportion of verbal versus nonverbal subjects who endorsed experiencing specific barrier to care; χ^2.

Supplemental Information, Supplemental Table 10). No significant association was observed between the IQ of children with ASD and (1) family income above versus below the median income of this group (P = .88), (2) the mother having versus not having a college degree (P = .07), or (3) estimated gestational age at birth before versus after 37 weeks (P = .93). Associations between IQ and clinical symptom burden were modest (P values between 0.06 and 0.91) (see Supplemental Table 11), with the exception of disproportionately more social-communication (but not restrictive or repetitive) symptoms among children deemed cognitively untestable ($P < .002$). Finally, 33.8% of the children with ID had histories of delay in age of first walking (defined by age of first walking ≥16 months by maternal report), in comparison with 18.2% of children with ASD only (odds ratio 2.3, $P < .001$). The mean age of first walking was 14.4 months (±6.1).

When restricting the sample to children diagnosed before 96 months and considering the complete set of predictors for IQ (ie, model 4 in hierarchical regression analyses), only 2 independent variables emerged as significant: (1) age in months at time of ASD diagnosis, with earlier diagnosis predicting lower IQ; and (2) delay in age of first walking (Table 5, IQ proxy model 4). The full model for IQ explained 16.6% of variance ($P < .001$), with age at time of diagnosis accounting for 3.8% of variance (P = .03) and delay in age of first walking accounting for 9.0% of variance ($P < .001$). We subsequently examined the association among these predictors and other parameters of clinical severity. Considering the complete set of predictors for social and adaptive outcomes on the Vineland-II, there was no association with timing of diagnosis. Retrospective reports of ASD severity emerged as a significant predictor for both social and adaptive outcomes, and delay in age of first

TABLE 4 Correlations Between Participants With ASD IQ, First-Degree Relatives IQ, Timing of Diagnosis, and Services and Demographics

	1	2	3	4	5	6	7	8	9
1. Average of parental IQ (n = 163)	—	—	—	—	—	—	—	—	—
2. Participants with ASD IQ (n = 250)	0.1	—	—	—	—	—	—	—	—
3. Non-diagnosed sibling IQ (n = 90)	0.2	−0.1	—	—	—	—	—	—	—
4. Age at diagnosis (n = 267)	−0.1	0.2*	−0.1	—	—	—	—	—	—
5. Age at first services (n = 235)	−0.1	0.3**	−0.1	0.5**	—	—	—	—	—
6. Participants with ASD SRS score (n = 260)	−0.1	−0.0	0.0	0.1*	0.0	—	—	—	—
7. Mother IQ (n = 162)	0.9**	0.1	0.1	−0.0	0.0	0.0	—	—	—
8. Father IQ (n = 135)	0.8**	−0.0	0.2	−0.1	−0.1	−0.2	0.4**	—	—
9. Family income (n = 241)	0.2*	0.1	0.1	−0.1	−0.1	−0.1	0.2*	0.2*	—
10. Mothers education level (n = 251)	0.3**	0.2*	0.3*	−0.1	−0.1	−0.1	0.3**	0.3**	0.6**

SRS, Social Responsiveness Scale; —, value provided below the diagonal.

* Indicates P value significant at .05 level (2-tailed).

** Indicates P value significant at .01 level (2-tailed).

walking was a significant predictor for adaptive outcomes (Table 5). Corresponding analyses were conducted for the full sample (not restricted to diagnosis before 96 months), the subset of subjects who were verbal, and the subset of subjects who were verbal and diagnosed before 96 months (results of which are reported in Supplemental Tables 12–14), and did not reveal any substantially discrepant patterns of association.

DISCUSSION

Within a sample of geographically diverse AA children with ASD, whose average age of diagnosis by parent-report was comparable to that documented in the CDC's epidemiological surveillance program, we documented substantial delays in ASD diagnosis. Parents in our sample reported sharing concerns about their children's development with a professional, on average 3 years before an ASD diagnosis was made, and 7 months earlier than in the 2011 Survey of Pathways to Diagnosis and Services (N = 1287).[11] Delays in diagnosis occurred despite the fact that the vast majority of the children in our sample had health insurance. Within this sample, earlier diagnosis was associated with lower IQ, which is consistent with clinical observations that children with more severe developmental delays are brought to clinical attention earlier. However, most children in the sample were diagnosed after the age of 4 years and beyond the period when early developmental therapies (typically delivered through part C interventions in the United States) are initiated to ameliorate the disability associated with ASD.

The cognitive outcomes of children with ASD in our sample, 35.2% of whom qualified for a diagnosis of ID, were not associated with gestational age at birth, family income, or the variation in IQ of first-degree relatives, all of which are associated with cognitive outcome in the general population. Therefore, the pronounced disparity in ID comorbidity between AA (44%) and NHW (22%) documented in US surveillance data for children with ASD[1] cannot be reasonably accounted for by these factors. The persistence of an unexplained excess of ID comorbidity of this magnitude in the AA population constitutes an urgent public health concern. If it is the case that delays in diagnosis (well documented here), compounded by poorer access to intervention services of reasonable quality (well documented in previous research), contribute to this disproportionate burden of ID comorbidity, it is incumbent upon insurers and health systems to resolve these issues as a first approach to ameliorating this serious health disparity.

Aside from the timing and quality of intervention, there are other factors that may differentially influence cognitive outcome across children of varying race and ethnicity. We identified 1 child out of 8 presumed to have ID within the CDC surveillance system and coenrolled in both studies who tested within the normal range of nonverbal intelligence. This raises the possibility that AA children with ASD may be disproportionately assumed to have ID and diagnosed as such without adequate psychometric confirmation. Such misclassification itself can contribute to disparities in appropriate intervention, but the frequency observed in this study would not account for the majority of excess ID burden among AA children with ASD.

The proportion of our consecutively ascertained AA subjects with delay in age of first walking (23.5%) was slightly higher than that observed in a previously published, predominantly white ASD cohort oversampled for comorbid ID[12]; both studies revealed an odds ratio of 2.3 for the relationship between early delay in walking and ID comorbidity, and in this study, delayed walking accounted for 9% of the variation in later cognitive outcomes of the children. As suggested in unselected cohorts of children with ASD, however, the frequency of delay in age of first walking is approximately equivalent for white and AA children diagnosed with ASD (Supplemental Table 15). If ancestry-based genetic interactions were responsible for a significant share of the disparity, we would expect the adverse cognitive outcomes of the children to reflect associations with other established biological correlates of ID in ASD, including prematurity, sex, and epilepsy, which were not observed.

TABLE 5 Hierarchical Regression Analyses Predicting Cognitive and Clinical Outcomes Within the Subsample Diagnosed ≤96 Months

Model	IQ Proxy				Vineland-II Social Outcomes				Vineland-II Adaptive Composite Outcomes			
	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
Intercept, β (SE)	58.3** (19.6)	76.1*** (20.8)	39.5 (26.0)	50.8* (25.0)	54.9*** (10.3)	84.4*** (9.1)	90.2*** (11.3)	91.9*** (11.3)	58.4*** (9.8)	88.3*** (9.4)	90.6*** (11.7)	93.3*** (11.6)
Income, β (SE)	1.9 (1.8)	1.5 (1.9)	1.1 (1.9)	0.1 (1.8)	1.0 (1.0)	0.4 (0.8)	0.4 (0.8)	0.3 (0.8)	0.7 (0.9)	−0.2 (0.9)	−0.2 (0.9)	−0.4 (0.9)
Sex: female, β (SE)	0.6 (4.7)	−1.2 (5.2)	−2.0 (5.2)	−2.6 (4.9)	−1.8 (2.4)	0.7 (2.2)	0.8 (2.2)	0.8 (2.2)	−1.1 (2.2)	1.2 (2.2)	1.3 (2.3)	1.1 (2.2)
Gestation:<37 wk, β (SE)	−3.1 (5.1)	−2.2 (5.2)	0.7 (5.3)	0.7 (5.0)	1.6 (2.5)	3.2 (2.1)	2.9 (2.1)	2.9 (2.1)	2.3 (2.4)	3.0 (2.2)	2.9 (2.2)	2.8 (2.2)
ASD severity, β (SE)	—	−0.6* (0.3)	−0.6 (0.3)	−0.5 (0.3)	—	−1.2*** (0.1)	−1.3*** (0.1)	−1.2*** (0.1)	—	−1.1*** (0.1)	−1.1*** (0.1)	−1.0*** (0.1)
Age of diagnosis, β (SE)	—	—	9.7* (4.2)	10.3* (4.0)	—	—	−1.6 (1.8)	−1.5 (1.8)	—	—	−0.6 (1.9)	−0.4 (1.8)
Walking onset: ≥ 16 mo, β (SE)	—	—	—	−14.8*** (4.0)	—	—	—	−2.6 (1.8)	—	—	—	−4.2* (1.8)
Observations	164	132	132	132	178	147	147	147	178	147	147	147
R^2	0.0	0.0	0.1	0.2	0.0	0.4	0.4	0.4	0.0	0.3	0.3	0.3
Adjusted R^2	−0.0	0.0	0.0	0.1	−0.0	0.4	0.4	0.4	−0.0	0.3	0.3	0.3

Age at time of diagnosis explained significant unique variance in IQ above and beyond a reduced model that contained income, gender, gestation duration, and retrospective reports of ASD severity ($\triangle R^2 = 0.04$, $P = .03$). Age of walking onset further accounted for unique variance in IQ ($\triangle R^2 = 0.09$, $P < .001$) and adaptive outcomes ($\triangle R^2 = 0.02$, $P = .03$). —, not applicable.

* $P < .05$.

** $P < .01$.

*** $P < .001$.

We note that the parent study through which these data were acquired, NIH MH100027, is designed to ensure that genetic research in autism is fully representative of human diversity, a major scientific motivation for which is to avoid gaps in identifying variable elements of causation that may be of particular importance to the overarching goal of developing interventions of relevance to all people.

Several study limitations should be noted. First, our sample did not include subjects of other racial and ethnic backgrounds (eg, Hispanic and Asian American and/or Pacific Islanders). Second, we did not include a comparably ascertained sample of NHW children from similar socioeconomic status backgrounds. We wish to emphasize that there does not exist an NHW sample phenotyped in the manner conducted within this cohort (simultaneous acquisition of event history calendar interview data and cognitive assessment of first-degree relatives). This within-cohort study was designed as a critical step in exploring targetable correlates of variation in timing of diagnosis and cognitive outcomes within a consecutively ascertained cohort representing the population disproportionately diagnosed with comorbid ID. Next critical steps should involve attempts to resolve intervention disparities as possible causes, as well as continued exploration of interactions between genetic background and specific biological susceptibilities to autism which is an objective of the parent study. Finally, there are also methodologic limitations of the US CDC epidemiological surveillance data (the most recent analysis of which critically contextualizes this study) for estimating both race and prevalence,[13] given that it is based on community diagnosis ascertained from school and medical records. This issue was mitigated, however, by examining and confirming a high level

of comparability of the characteristics of our study cohort (including ID comorbidity) with that of AA subjects identified in the CDC surveillance program and our collection of a large, diverse AA ASD sample with ancestry characterized by genotype, among whom correlates of cognitive ability were extensively examined within the sample.

CONCLUSIONS

With these findings, we highlight a pressing need to determine whether broad implementation of timely diagnosis, when coupled with high-quality early intervention, would reduce the proportion of AA children with autism and comorbid ID. Within our sample, variation in cognitive outcome was not explained by sociodemographic or familial factors that have been associated with variation in IQ, suggesting that excess ID in AA children with autism cannot straightforwardly be accounted for by these factors, or by overclassification of ID (which in and of itself would constitute a problematic disparity). A recent analysis of outcomes of young children receiving therapy based on applied behavior analysis demonstrated that greater intensity and duration of service were associated with clinically and statistically significant gains in cognitive capacity and executive skills.[14] An immediate public health and research priority is to explore the extent to which resolution of health disparities that compromise timely access to effective intervention can reduce deleterious effects on cognition that disproportionately accompany autism among AA youth.

ACKNOWLEDGMENTS

We acknowledge the efforts of the families who participated in this research program. We thank Marshalyn Yeargin-Allsopp, MD for her guidance during the development of the Diagnostic Odyssey Interview and the preparation of this article, and Catherine Rice, PhD for assistance with use of the CDC surveillance data in contextualizing the results of this data collection. We also wish to recognize MD and PhD candidate Simona Sarafinovska for her help with literature review.

ABBREVIATIONS

AA: African American
ADDM: Autism and Developmental Disabilities Monitoring
ADI-R: Autism Diagnostic Interview-Revised
ADOS: Autism Diagnostic Observation Schedule
ASD: autism spectrum disorder
CDC: Centers for Disease Control and Prevention
ID: intellectual disability
NHW: non-Hispanic white
NIH: National Institutes of Health
SCQ: Social Communication Questionnaire

Dr Klin drafted the initial manuscript, conceptualized and designed the study, secured funding, and assumed the role of principal investigator for data collection site; Dr Shattuck coauthored the Diagnostic Odyssey data collection instrument; Dr Molholm conceptualized and designed the study, secured funding, and assumed the role of principal investigator for data collection site; Dr Fitzgerald coordinated and supervised data collection and conducted analyses of data; Ms Roux coauthored the Diagnostic Odyssey data collection instrument; Dr Lowe coordinated and supervised data collection and conducted analyses of data; Dr Geschwind drafted the initial manuscript, conceptualized and designed the study, secured funding, and assumed the role of principal investigator for data collection site; and all authors critically reviewed and revised the manuscript and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2019-3629

Accepted for publication May 29, 2020

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: Dr Constantino receives royalties for commercial distributions of the Social Responsiveness Scale, Second Edition, from Western Psychological Services; Dr Saulnier receives royalties from Pearson Clinical and is a consultant to Ovid Therapeutics, Yamo Pharmaceuticals, and Holland Bloorview Kids Rehabilitation Hospital; Dr Geschwind is a consultant to OVID Therapeutics, Axial Therapeutics, Acurastem, and Falcon Computing; the other authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: This research was supported by US National Institutes of Health grant MH100027 to Dr Geschwind and colleagues, and HD087011, the Intellectual and Developmental Disabilities Research Center at Washington University in St Louis, to Dr Constantino; the other authors received no external funding. Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: Dr Constantino is author of the Social Responsiveness Scale-2, and Dr Saulnier is coauthor of the Vineland-3; the other authors have indicated they have no potential conflicts of interest to disclose.

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