Asthma and Allergies in Children With Autism Spectrum Disorders: Results From the CHARGE Study

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Abstract

Immune aberrations are often noted in children with autism spectrum disorder (ASD), but whether asthma and allergy are related to ASD is not well defined. This study examined asthma and allergies in association with ASD and phenotypic subsets. Participants were 560 children with confirmed ASD and 391 typically developing children from the CHildhood Autism Risks from Genetics and the Environment study. Maternally reported child asthma and allergy was compared between cases and controls, and in association with cognitive and behavioral test scores. Prevalence of asthma and overall allergies did not differ between cases and controls, but overall allergy in children with ASD was associated with higher stereotypy scores as measured by the Aberrant Behavior Checklist. In addition, reported food allergies were significantly associated with ASD (adjusted odds ratio = 2.23, 95% confidence interval 1.28, 3.89). Our results suggest food allergies and sensitivities may be more common in children with ASD, and that these issues may correlate with other behaviors.

Keywords

autism; asthma; allergy; food allergy

Introduction

Deficits in social functioning, communication, and language, and presence of restricted, repetitive behaviors define autism spectrum disorder (ASD); however, there is wide phenotypic variability in children diagnosed with ASD. A range of medical conditions also frequently co-occur in children with ASD. Aberrations in the immune system are one such problem frequently noted, including a history of frequent infections [Jyonouchi, Geng, Cushing-Ruby, & Quraishi, 2008], altered cytokine levels [Ashwood, et al., 2011], and increased prevalence of autoimmune conditions [Goines & Van de Water, 2010].

It is not clear whether other immune-mediated conditions, including asthma and allergies, are related to ASD. Two studies have suggested an increased prevalence of allergies in persons with autism, but lacked adequate control groups [Menage et al., 1992; Renzoni et al., 1995]. Two other reports found no difference in measured IgE levels (generally elevated in allergies) in children with autism [Bakkaloglu et al., 2008; Heuer et al., 2008], although sample sizes were small. Another study reported no difference in the prevalence of asthma or allergy in children with ASD when compared to the prevalence in the general population [Jyonouchi et al., 2008]. A link between food allergy specifically and ASD has been suggested as a potential underlying cause for the high prevalence of gastrointestinal problems in children with ASD [Jyonouchi, 2009]. However, few studies have explored these associations further.

Whether asthma and allergies correlate with behavioral and developmental phenotypes in ASD, including behavioral problems, cognitive scores, and subphenotypes, has also not been examined in depth. However, other immune aberrations, namely the presence of autoantibodies to cerebellar proteins, have been associated with lower adaptive and cognitive function scores in autism relative to affected children without these autoantibodies [Goines et al., 2011]. In addition, medical comorbidities like allergies in the general population are often related to increased irritability and poorer functional outcomes in children [Jyonouchi, 2010], and within ASD other medical comorbidities, such as gastrointestinal symptoms, have been shown to predict higher levels of irritability, social withdrawal, hyperactivity, and stereotypies [Chaidez, Hansen, & Hertz-Picciotto, 2013]. Whether allergies and asthma may further and similarly impair the level of functioning in children with ASD is not clear. It is also unclear the extent to which gastrointestinal problems, which are common in children with autism [Chaidez et al., 2013], may relate to immune issues like asthma or allergy, or whether such issues may account for previously reported associations with food allergies in particular.

Given the inconsistencies and limitations in prior work, we sought to determine whether (1) asthma and allergies are more common in children with ASD and (2) asthma and allergies are associated with subphenotypes or cognitive and behavioral scores in children with and without ASD. To address these questions, we used data from a large population-based case-control study with detailed diagnostic and exposure assessments. In a subset of our study group, we also examined IgE levels.

Methods

Study Population

Participants of this study are part of the CHildhood Autism Risk from Genetics and the Environment (CHARGE) study, an on-going, large, population-based case-control study drawn from several regions of California [Hertz-Picciotto et al., 2006]. Study inclusion criteria are as follows: children aged 2–5 at study enrollment, living with at least one biological parent, English or Spanish speaking parent, born in California, and residing within one of the CHARGE study catchment areas. Children with autism (AU) were identified through the California Department of Developmental Services (DDS), referrals from health and service providers, or self-referrals, and healthy controls through state birth

files. Controls were frequency-matched on age, sex, and geographic area to AU cases. DDS diagnoses of autism were confirmed at the UC Davis MIND Institute by conducting the Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview-Revised (ADI-R). All clinicians conducting assessments have achieved research reliability on the instruments they administer.

The following definitions were used for diagnoses: (a) autism: meeting criteria on the communication, social, and repetitive behavior domains of the ADI-R, with onset before 36 months, and meeting communication and social interaction cut-offs of the ADOS Module 1 or 2; (b) autism spectrum: meeting either the communication or social interaction domain of the ADI-R, with onset before 36 months, and being within two points of meeting criteria in the other domain, and meeting the ASD cut-off for social and communication totals of the ADOS. For this analysis, we defined ASD cases as the combined group of children with AU and children with autism spectrum. In the children recruited as general population controls, the Social Communication Questionnaire (SCQ) was used to screen for autism spectrum symptoms, with a cut-off score of 15; if autism was suspected, the ADI-R and ADOS were conducted. For the current analysis, controls, designated "typically developing" (TD), were defined as children recruited from the general population who scored 70 or higher on the Mullen Scales of Early Learning (MSEL), 70 or higher on the Vineland Adaptive Behavior Scales (VABS), and 14 or lower on the SCQ. We included only those children meeting clinical-assessment cut-offs for AU, ASD, or TD.

Exposure Assessment

Information on child asthma and allergies was collected through maternal report on an Environmental Exposure Questionnaire (EEQ), a detailed family/child medical history, and an autoimmune survey. The EEQ, administered by trained interviewers over the phone, asked mothers whether their child had taken medication for asthma and allergies from birth until study assessment, and at what age(s) the child had these conditions. The medical history, administered by a physician to mothers, asked whether the child had any environmental, medication, food, skin, or other allergies (and if so, to further specify type/ trigger). Finally, the autoimmune survey included a question asking mothers whether their child had asthma, and if so, the age at onset of the condition. For the purpose of these analyses, children were considered as having allergies or asthma if reported on any of these sources, unless the mother reported medication use for the condition on the EEQ but reported no asthma or allergies on the medical history and autoimmune survey. Secondary analyses examined the effect of including those reporting only medication use for these conditions.

In a subset of 229 children in this study group, including 136 cases and 93 controls, IgE levels had been measured. Laboratory assessment of IgE levels in this population has been previously described [Heuer et al., 2008].

Statistical Analysis

All analyses were conducted using SAS 9.3. Frequency of asthma and allergies, overall and by type, were compared between cases and controls using chi-squared test. Logistic

regression was used to calculate the odds of asthma, and of allergies, in association with ASD. In multivariate models, we included CHARGE study matching factors (child year of birth, sex, and regional area), and examined the effect of adjustment for the following variables based on a priori knowledge: maternal asthma/allergy, child recurrent infections in early life, maternal age, breastfeeding, race, and maternal smoking. We utilized inverse-probability sampling weights, derived based on sociodemographic characteristics of the source population, to account for selection into the CHARGE study, in weighted analyses using Proc Survey Logistic in SAS. (Specifically, the following variables were used in calculating the probability of selection to derive weights, conditional on recruitment group: mother's education, age, country of birth, insurance status at delivery, and race/ethnicity). Based on a priori knowledge and associations with both ASD and child asthma/allergy, the final analysis models adjusted for matching factors and child recurrent infections, and additionally, in our analyses of child asthma, maternal smoking.

Mean differences of child cognitive and behavioral scores on the ABC, MSEL, VABS, and (for cases only) ADOS and ADI-R were compared between children with and without asthma and allergy, stratified by case status, using Wilcoxon rank sum tests. Adjusted analyses of the association between asthma and allergies and scores, with covariate assessment and weighting as above, were conducted using linear regression.

Sensitivity and Supplemental Analyses

In secondary analysis of plasma IgE measurements, *T*-tests for the difference in means were conducted to compare cases with controls, and those with vs. without allergies. IgE values were log-transformed prior to these comparisons due to their distribution. Finally, due to previous suggestions of associations between gastrointestinal problems and food allergies in children with ASD, we also examined whether these symptoms, as reported on a gastrointestinal survey completed by mothers, were associated with allergies in our study group. A separate paper conducted by researchers in our group examines GI problems in autism in more detail [Chaidez et al., 2013].

Results

Basic characteristics of the study population are shown in Table 1; 560 cases and 391 controls were included in these analyses. Control mothers were more likely to have higher education, less likely to have smoked regularly, and slightly more likely to be Caucasian; analyses, therefore, tested the effect of adjusting for sociodemographic factors. Prevalence of asthma was the same in cases and controls (16%, $P = 0.93$); prevalence of overall allergies was high, and prevalence was similar in cases compared with controls (42% and 40%, respectively; $P = 0.39$). Regarding overlap of these conditions, 10% of cases and 9% of controls were reported to have both asthma and allergy; this difference was not statistically significant ($P = 0.65$).

When examining types of allergies in unadjusted analyses, mothers of cases were significantly more likely to report food and environmental allergies, and were also slightly more likely to report multiple allergies (Fig.1). In all children, those with food allergies were most likely to have another type of allergy reported (77%), with environmental allergies

being the most commonly co-occurring. For the other types of allergies, 55% of individuals with skin allergy, 49% of individuals with medication allergies, and 36% of individuals with environmental allergy were reported to have another type of allergy as well. The majority of children with allergies did not have information available on trigger/allergen. However, among individuals specifying this information, the most common triggers by allergy type were as follows: for food allergies, milk/dairy, nuts, and fruits; for environmental allergies, hayfever/seasonal allergy, grass, and animals; for medications, the majority reported were amoxicillin or penicillin; skin allergy trigger information was not available for most participants.

In adjusted analyses, the significant association with food allergies persisted, with cases being approximately twice as likely to have had food allergies reported (adjusted OR = 2.23, 95% CI 1.28, 3.89). Other associations were nonsignificant, although skin allergy demonstrated a borderline-nonsignificant inverse association with ASD (Table 2). Results were similar across modeling strategies (adjusted for matching factors only, adjusted for additional potential confounders, and with use of inverse probability weights), suggesting selection and confounding did not greatly impact these associations (Table 2). Since family history is a strong predictor of risk for both asthma and allergies in the children, and since maternal asthma and allergies have been associated with autism in at least one study [Croen, Grether, Yoshida, Odouli, & Van de Water, 2005], we examined the effect of adjustment for maternal asthma and allergy. Neither was independently associated with ASD in our population, and adjustment for these maternal conditions did not alter the results comparing child asthma and allergy in cases vs. controls.

Presence of asthma or allergies in both cases and controls was associated with modestly lower scores (indicating poorer functioning) when comparing means on the MSEL and VABS, and modestly greater impairment on the ABC, and for cases only, on the ADI-R. However, with few exceptions, these associations were within expectation of random fluctuations. Specifically, among cases, those with allergy and asthma had greater stereotypies as measured by the ABC and ADI-R, while other comparisons were not statistically significant. In adjusted analyses, child allergy was associated with approximately a one point increase in stereotypy score in cases, as measured on either the ABC stereotypy subscale or the ADI-R C domain (Table 3). Other associations were not significant ($P < 0.05$) in adjusted analyses.

Sensitivity and Supplemental Analysis Results

In the subgroup of children with measured IgE levels, mean IgE was moderately higher in cases as well as in children with allergies, but these differences were not statistically significant according to T-tests of log-transformed values ($P = 0.19$ and $P = 0.41$ respectively).

Reported GI problems (including diarrhea, pain on stooling, blood in stool, vomiting) and diagnosis of gastrointestinal disorders (including gastroesophageal reflux disease, Celiac disease, and others) were slightly more common in children with food allergies than in those without (Table 4); likewise, the reported prevalence of any allergy was higher in children with GI diagnoses (73% of those with reported GI diagnoses also had reported allergies).

Only GI diagnosis (but not broader GI problems examined) in the overall study group and in cases, specifically, were more common in those with any allergy compared to those without. When adjusting the association between ASD and food allergy for presence of GI disorders/ diagnoses, the association was slightly attenuated, but remained significant (adjusted OR = 1.94, 95% CI 1.09, 3.48). The association was similarly attenuated but remained significant when conditioning on absence of GI diagnoses (association between food allergies and ASD in children with no reported GI disorders OR = 1.84, 95% CI 1.01, 3.39). Likewise, the association between GI diagnosis and ASD was attenuated but remained significant when adjusting for food allergy (OR not adjusted for food allergy 5.5, 95% CI 2.18, 13.8; adjusted for food allergy OR = 3.6, 95% CI 1.35, 9.43, or among those without food allergy OR = 3.5, 95% CI 1.13, 10.6). Thus, while there was considerable overlap between food allergies and GI problems, the association between food allergies was not due solely to GI problems, and vice versa.

When including an additional 59 women who reported use of medications for their child's allergies, but reported no allergies on other assessments, results of all analyses were similar, although somewhat stronger for overall allergies (adjusted OR = 1.29, 95% CI 0.95, 1.77). When exploring reported use of other medications in this population to address whether treatments could potentially influence the child's results on cognitive and behavioral testing, we found that the majority of medications reported were asthma medications, over-the-counter drugs such as acetaminophen, and vitamins. Less than 1% of participants were reported to be taking psychiatric medications (Ritalin, valium), and exclusion of these individuals did not alter findings.

Discussion

In this large population-based case control study, we found no evidence for a difference in the prevalence of asthma between children with ASD and TD controls. Prevalence of allergies was slightly higher in case children, however, and food allergies in particular were reported more commonly in children with ASD than in TD children. We also found evidence that presence of allergies may be associated with slightly higher stereotypy scores in children with ASD, although the increase was modest (less than half of a standard deviation change).

Prior studies examining allergies in autism have reported conflicting results and have been methodologically limited. Of two reports suggesting a high prevalence of allergies in children with autism, one was a case report ($n = 6$), while the other included just 43 cases and used a group of 43 controls with various forms of mental retardation, some of which are associated with higher rates of autism [Menage et al., 1992; Renzoni et al., 1995]. A third study suggested a high prevalence of allergies in Asperger syndrome, but again only included a small number of cases ($n = 15$) [Magalhaes et al., 2009]. Another investigation, which included 30 children with ASD, reported a much higher prevalence of atopic features in family members of cases as compared to controls, but no difference between the affected and comparison children in presence of asthma, allergies, or in serum tests of common antigens [Bakkaloglu et al., 2008]. Two other recent studies reported no differences in measured IgE levels in children with and without autism [Bakkaloglu et al., 2008; Heuer et

al., 2008], although non-IgE mediated allergies would not be captured by this analysis. Our finding of no difference in the prevalence of overall allergy between ASD cases and TD controls is in agreement with these more recent studies, one of which was a laboratory analysis of a subset of CHARGE participants, as well as an additional study suggesting that ASD allergy prevalence is in line with that of the general population [Jyonouchi et al., 2008]. However, we did note some differences in types of allergies, further discussed below. Earlier reports of increased allergy prevalence in ASD may have been due to chance fluctuations in small samples, differences in the types of allergies included, or biases in selection, such as use of clinic-referred populations.

Our work did suggest that food allergies in particular were more common in children with ASD, and this association was statistically significant. This finding is supported by prior work noting the frequent gastrointestinal problems and food sensitivities in children with autism [Jyonouchi, 2009]; these same authors also reported a higher prevalence of food allergies in 133 ASD cases as compared to 43 controls [Jyonouchi et al., 2008]. Alternatively, it is also possible that in both studies, parents have reported sensitivities as allergies, and the GI symptoms may be a result of heightened sensitivities to certain food antigens in children with ASD. Jyonouchi and coworkers have also suggested differences in the relationship between food allergies and autism according to IgE mediated and non-IgE mediated allergies: specifically, that non-IgE mediated allergies are positively associated with autism. This may explain previously reported findings of no difference in IgE levels between cases and controls. In our study, we did not examine IgE-mediated vs. non-IgE mediated food allergy, as information on type/trigger of food allergy was not specified for the majority of participants and this would help to classify such comparisons. Food allergy in our study thus likely included both IgE-mediated and non-IgE mediated allergy, or both true food allergy as well as food sensitivity; however, we believe both may be meaningful, particularly if there are differences in cases and controls and those differences relate to functioning. Mothers in our study may have reported food sensitivities as food allergy, and it is possible that mothers of children with ASD are more attuned to these food issues than mothers of TD children. Finally, while food allergies demonstrate considerable overlap with GI problems, our stratified and adjusted analyses suggested that both allergy and GI problems may have independent associations with ASD. Given the small sample sizes of prior studies, additional examination of food allergies and sensitivities is needed to determine whether and how these issues relate to ASD.

We also noted a slight decrease in skin allergies among ASD cases. Future studies should examine this and other types of allergies within ASD to confirm our findings, to examine the possibility that affected children might be protected against certain types of allergies and more prone to others.

There is little prior work examining asthma in children with ASD. We found no evidence for an association between asthma and ASD in our study. Similarly, a previous study conducted by Jyonouchi and coworkers also found no difference between the prevalence of asthma in their case group and the general population prevalence, although their sample size was small [Jyonouchi et al., 2008]. Our work also did not find statistically significant differences in child cognitive and behavioral scores according to asthma, although there was a

nonsignificant trend toward poorer functioning in those with asthma, suggesting that the condition may have minor effects on cognitive performance and behaviors such as irritability, hyperactivity, and stereotypies.

Medical comorbidities have substantial clinical impacts on outcomes and level of functioning in children with ASD, and one of our study goals was to determine the impact of asthma and allergy on a range of cognitive and behavioral test scores. Although we observed few notable associations, our results suggest allergies could be related to repetitive behaviors/stereotypies. In addition, children with allergies and asthma demonstrated modestly lower functioning, and modestly greater deviant impairments, than children without these issues. These trends were observed in both case and control children, but were somewhat stronger overall in children with ASD.

Other studies have supported the finding that asthma and allergies may negatively impact child functioning. Large, general population studies have found asthma to be associated with poorer standardized scores on math and reading tests, worse academic performance, and higher school absence [Kohen, 2010; Moonie, Sterling, Figgs, & Castro, 2008]. Allergies have also been reported to impact quality of life and social functioning in the general population [Jirakova, Vojackova, Gopfertova, & Hercogova, 2012]. Overall, these results are in accordance with our findings. While causal relationships between immune impairments and behaviors have yet to be fully determined, and are likely to be quite complex, associations of asthma and allergies with cognitive abilities, adaptive functioning, and other behaviors in children with ASD, may be a marker of aberrant immune development rather than a direct pathway. Differences could also be related to management of symptoms. Although few statistically significant associations were seen in our analyses of these scores with asthma and allergy, the pattern of results suggested potential minor effects that should not be completely disregarded.

One limitation of our work is that we relied on maternal reporting to determine presence of allergies and asthma. Thus, we cannot rule out potential misclassification, and biased reporting is possible. We used trained interviewers and physicians to conduct detailed interviews, to probe and extract information from participants, but both Type I and Type II errors are possible. Our results did not suggest differences in the presence of asthma and allergies overall between cases and controls, but food allergies were more commonly reported among cases. As stated previously, it may be that case mothers are more sensitive to or aware of food allergies and sensitivities, particularly given the popularity of alternative therapies such as gluten-free diets. Future work should attempt to obtain medically validated allergy information, including type of allergies and triggers, as these may differ according to ASD.

Another potential limitation is that our study included young children—aged 2–5 at study assessment. Multiple studies have demonstrated an increase in the prevalence of asthma and allergies with child age [Amin & Davis, 2012; Rona et al., 2007]. Thus, some children may have yet to develop asthma/allergies, and therefore, these results may not generalize to older populations. Although unlikely in our study, we also cannot rule out a potential effect of medication use on cognitive and behavioral testing. Types of medications used in this young

population were primarily over the counter and vitamins, and sensitivity analyses suggest this did not impact on our findings; however, medications could play a role in other study populations with higher use of psychotropic medications.

Despite these limitations, this study has a number of strengths, including a larger sample size than most prior studies examining asthma and allergy in children with autism. Another key strength of our study was the use of detailed diagnostic assessments, conducted by trained and research-reliable clinicians; outcome misclassification was, therefore, highly unlikely.

A growing body of evidence has linked immune issues in children with ASD. The current study adds to that literature by suggesting that asthma and allergies, overall, are not more prevalent in young children with autism relative to TD controls. However, continued research should examine the potential underlying reasons for the high prevalence of food allergies/sensitivities in children with ASD, as well as potential relationships between immune aberrations, including asthma and allergies, with subphenotypes and behaviors like stereotypies in children with ASD.

Acknowledgments

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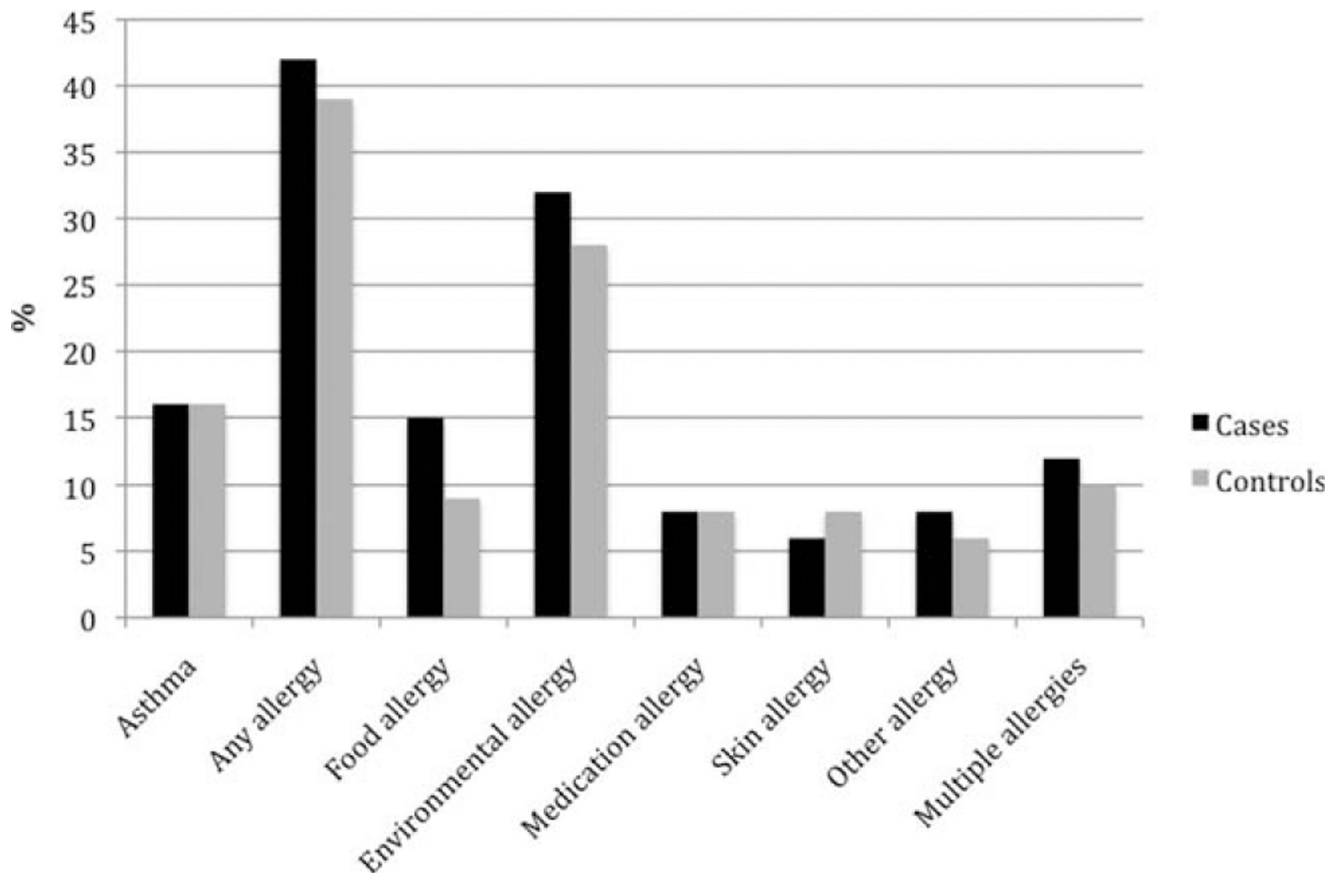
Figure 1.
Prevalence of maternally reported asthma and allergies in children with typical development (controls) and with ASD (cases) from the CHARGE study. Case asthma and allergy % shown in black, controls in grey. Allergy categories are not mutually exclusive. "Other allergy" refers to individuals reporting allergies not falling into the specified categories, while "multiple allergies" refers to those reporting in more than one category. Sixty-four cases (24% in cases with allergy) and 47 controls (26% in controls with allergy) did not report allergy type.

Table 1.

Basic Characteristics of the Study Population

	ASD Cases *n* = 560	Typically developing controls *n* = 391
	Mean (std)	
Maternal age	31.1 (5.5)	31.0 (5.8)
Paternal age	33.6 (6.4)	33.5 (7.0)
Child year of birth	2003 (2.2)	2002 (2.3)
Mean duration breastfed (months)[(*)]	6.7 (7.1)	7.8 (6.3)
	n (%)	
Government program insurance status at delivery[(*)]	111 (20%)	60 (15%)
Maternal education level[*]		
High school or less	82 (15%)	62 (16%)
Some college	231 (41%)	130 (33%)
College or graduate degree	246 (44%)	198 (51%)
Maternal race		
Caucasian	333 (59%)	251 (64%)
Hispanic	139 (25%)	83 (21%)
Other	88 (16%)	57 (15%)
Maternal smoking-ever regular smoker[*]	131 (23%)	70 (18%)
Maternal asthma	93 (17%)	74 (18%)
Maternal allergies (any)	297 (56%)	223 (59%)
Male child	482 (86%)	326 (83%)
Child recurrent infections[a*]	42 (8%)	15 (4%)

[a]From birth to present, as reported in child medical history.

[(*)]$P < 0.1$,

[*]$= P < 0.05$,

[**]$= P < 0.01$.

Table 2.

Risk of Child Asthma and Allergies according to Autism Spectrum Disorder

	Odds ratio (95% confidence interval)		
	Model 1	**Model 2**	**Model 3**
Asthma	0.94 (0.65, 1.35)	0.84 (0.56, 1.28)	0.86 (0.57, 1.30)
Allergy	1.10 (0.83, 1.46)	1.17 (0.86, 1.61)	1.15 (0.84, 1.57)
Food allergy	1.83 (1.13, 2.97)	2.25 (1.30, 3.90)	2.23 (1.28, 3.89)
Medication allergy	1.01 (0.60, 1.71)	1.15 (0.67, 1.96)	1.08 (0.62, 1.87)
Environmental allergy	1.17 (0.86, 1.59)	1.28 (0.91, 1.80)	1.24 (0.88, 1.75)
Skin allergy	0.42 (0.23, 0.77)	0.55 (0.29, 1.02)	0.56 (0.30, 1.06)

Table shows association between child asthma and allergies (the outcomes) in association with case status.

Model 1 is unweighted (does not account for study weights that take into account demographic selection factors), from logistic regression, adjusted only for study matching factors (child year of birth, regional catchment area, and sex).

Model 2 is from weighted logistic regression, accounting for study weights, and adjusted for study matching factors.

Model 3 is from weighted logistic regression, accounting for study weights, and adjusted for study matching factors, child recurrent infections in early life, and (for asthma only) maternal smoking. Additional adjustment for maternal allergies or asthma, maternal age, or breastfeeding did not materially alter results.

Table 3.

Child Asthma and Allergies in Association With Cognitive and Behavioral Scores

	Estimate (std error)		
	Model 1	Model 2	Model 3
Asthma			
ABC stereotypy			
Cases	0.98 (0.5) [(*)]	0.3 (.6)	0.05 (.6)
Controls	−0.01 (0.05)	−0.03 (0.03)	−0.02 (0.03)
ABC irritability			
Cases	1.25 (1.1)	0.13 (1.2)	0.15 (1.1)
Controls	1.16 (.5) [*]	0.8 (.7)	1.1 (.7)
ABC hyperactivity			
Cases	1.5 (1.4)	−0.4 (1.7)	−0.1 (1.6)
Controls	1.1 (.7)	0.5 (.9)	0.75 (.9)
Allergy			
ABC stereotypy			
Cases	1.01 (.4) [*]	0.96 (.47) [*]	0.81 (.47) [(*)]
Controls	−0.02 (0.04)	0.005 (0.04)	0.005 (0.04)
Mullen expressive language			
Cases	0.24 (0.9)	−0.05 (0.8)	0.02 (0.8)
Controls	2.5 (1.2) [*]	1.6 (1.4)	1.6 (1.4)
ADI-R social domain (cases only)	0.92 (.4) [*]	0.91 (0.5) [(*)]	0.90 (0.5) [(*)]
ADI-R RRB domain (cases only)	0.55 (.2)	0.58 (.22)	0.58 (.22) [**]

ABC = Aberrant behavior checklist. ADI-R = Autism diagnostic interview-revised. RRB = Restricted repetitive behaviors/stereotypy domain.

Table presents the adjusted linear regression results of those factors for which significant crude associations were found; associations of child asthma, and allergies with other cognitive and behavioral scores were nonsignificant. Crude score differences are shown in Supporting Information Table 1.

[(*)] = $P < 0.1$,

[*] = $P < 0.05$,

[**] = $P < 0.01$.

Additional adjustment of Model 3 for maternal race or education did not alter results.

As for Table 2: Model 1 is unweighted (does not account for study weights that take into account demographic selection factors), from logistic regression, adjusted only for study matching factors (child year of birth, regional catchment area, and sex). Model 2 is from weighted logistic regression, accounting for study weights, and adjusted for study matching factors. Model 3 is from weighted logistic regression, accounting for study weights, and adjusted for study matching factors, child recurrent infections in early life, and (for asthma only) maternal smoking. Additional adjustment for maternal allergies or asthma, maternal age, or breastfeeding did not materially alter results.

Table 4.

Prevalence and Overlap of Child Conditions

	All children	Cases	Controls
Asthma prevalence	16%	16%	16%
In those with GI diagnosis	25%	24%	33%
In those with Regular GI problems	19%	18%	17%
In those with Allergy	23%	23%	23%
Allergy prevalence	47%	48%	45%
In those with GI diagnosis	73%	74%	*67%*
In those with Regular GI problems	50%	51%	47%
Food Allergy prevalence	12%	15%	9%
In those with GI diagnosis	34%	38%	*16%*
In those with Regular GI problems	18%	18%	22%
GI diagnosis prevalence	5%	7%	2%
In those with Allergy	8%	11%	*2%*
In those with Food allergy	14%	18%	*4%*
In those with Medication allergy	11%	16%	*4%*
In those with Environmental allergy	7%	10%	*2%*
In those with Skin allergy	10%	*19%*	*4%*
Regular GI problems prevalence	39%	48%	15%
In those with Allergy	41%	58%	16%
In those with Food allergy	59%	67%	38%
In those with Medication allergy	37%	50%	18%
In those with Environmental allergy	41%	56%	18%
In those with Skin allergy	35%	67%	*11%*

Shaded rows display overall prevalence in study group.

Italics indicates % is based on exposed *n* < 5. Prevalence of asthma among those with different types of allergies was similar to the prevalence in those with any allergy.