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Association between atopic dermatitis and attention deficit hyperactivity disorder in U.S. children and adults*

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Summary

Background—Atopic dermatitis (AD) is associated with chronic itch, allergic disease and sleep disturbance, all of which might increase the risk of attention deficit (hyperactivity) disorder (ADD/ADHD). Previous analyses have found a consistent association between AD and ADD/ADHD, although the underlying factors contributing to such an association remain underexplored. Additionally, the relationship has been underexplored in adults.

Objectives—To determine if childhood and adult AD and AD severity are associated with ADD/ADHD and to delineate the factors contributing to such an association.

Methods—We analysed data on 354 416 children aged 2–17 years and 34 613 adults age 18+ years from 19 U.S. population-based surveys, including the National Health Interview Survey 1997–2013 and the National Survey of Children's Health 2003/4 and 2007/8.

Results—In multivariate models adjusting for age, sex, sociodemographics, allergic disease and healthcare utilization, AD was associated with ADD/ADHD in both children [adjusted odds ratio (95% confidence interval), 1·14 (1·03–1·26)] and adults [1·61 (1·25–2·06)]. Children with both severe AD and only 0–3 nights of adequate sleep per week had much higher odds of ADD/ADHD

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website

Conflicts of interest

None declared.

[16·83 (7·02–40·33)] than those with 0–3 nights of adequate sleep per week [1·83 (1·47–2·26)] or mild–moderate AD alone [1·56 (1·22–1·99)]. AD was most strongly associated with severe ADHD. AD unaccompanied by other allergic disease was also associated with increased risk of ADD/ADHD in children. Among children with AD, history of anaemia, headaches and obesity were associated with even higher odds of ADD/ADHD. Asthma, insomnia and headaches increased the odds of ADHD in adults with AD, although underweight body mass index was protective.

Conclusions—Atopic dermatitis is associated with increased odds of ADD/ADHD in adults and children. Several factors increase the risk of ADHD in adults and children with AD.

Atopic dermatitis (AD) is a chronic inflammatory skin disorder associated with intense itch and sleep disturbance.[1] These symptoms may lead to distraction and difficulties with attention and concentration. Indeed, several previous studies and a systematic review have found associations between childhood AD and attention deficit (hyperactivity) disorder (ADD/ADHD)[2–9] and attention problems.[10,11] However, the relationship between adult AD and ADD/ADHD has been underexplored. Furthermore, the risk factors underlying the association between AD and ADD/ADHD have not been fully explored. One study has implicated sleep disturbance as a contributing factor,[12] and two studies have implicated AD severity. [4,6] Childhood AD is also associated with multiple allergic and nonallergic comorbidities that might further contribute to the increased risk of ADD/ADHD, including obesity,[13–15] anaemia,[16] headaches,[17] asthma[18] and allergic rhinitis.[18] We hypothesized that AD is independently associated with increased risk of ADD/ADHD in children, and that disease severity and sleep disturbance act in concert to increase the risk of ADD/ADHD. However, the relationship between AD and ADD/ADHD is more complex and there are likely to be other factors that contribute to such increased risk. Children with AD who develop ADD/ADHD may have a more severe phenotype and be more likely to have their AD persist into adulthood. The present study analysed 19 U.S. population-based surveys to determine if there is an association between AD and ADD/ADHD in children and adults and also to delineate the underlying clinical factors and comorbidities that contribute to such an association.

Methods

Study sources

Cross-sectional data were assessed from 19 population-based surveys, each assembled by the National Center for Health Statistics (NCHS), including the 1997–2013 National Health Interview Survey (NHIS) and the National Survey of Children's Health (NSCH) 2003/4 and 2007/8. The characteristics of each survey are described in Supplementary Table S1 (see Supporting Information). Briefly, the NSCH were a set of telephone-based surveys collected by screening randomly generated households for the presence of children under age 18 years, for the purpose of estimating the prevalence of child health issues. The NHIS is a yearly survey collected in person by trained interviewers using computer-based methods for the purpose of monitoring the health of the noninstitutionalized U.S. population of adults and children. Common to all surveys is a multi-stage area probability sampling design that utilizes data from the U.S. Census Bureau including age, sex, race, ethnicity, household size

and educational attainment of the most educated household member. Sample weights were created by the NCHS allowing for frequency and prevalence estimates that are representative of each state's population of noninstitutionalized children or adults. In this study, frequency and prevalence estimates presented in analyses of single surveys and in pooled analyses of multiple surveys of either NHIS ($n = 17$) or NSCH ($n = 2$) reflect this complex weighting process, as sample weights could be combined due to similarities in survey methodology. In pooled analyses using data from both NHIS and NSCH, unweighted data are presented. This study was approved by the Institutional Review Board at the Northwestern University.

Associations with atopic dermatitis and attention deficit (hyperactivity) disorder

Associations of both AD and ADD/ADHD were examined in children aged 2–17 years, including sex, age, race, household income, highest level of household/parental education, birthplace in the U.S. or elsewhere and insurance coverage. Associations between caregiver-reported history of childhood AD (19 surveys) and AD severity (one survey), and self-reported history of adult AD (one survey) and ADD/ADHD were examined both for each individual survey and in pooled analyses. To isolate the effect of AD from other allergic diseases, we also stratified children with AD only, asthma only, hay fever only, and each combination of the three, and examined the association of each group with ADD/ADHD. Finally, we examined the effect of anaemia, headaches and obesity on the risk of ADD/ADHD in children with AD, and additionally, the effect of insomnia in adults with AD.

Data analysis

All data analyses and statistical processes were performed using the SURVEY procedures in SAS version 9.4 (SAS Institute, Cary, NC, U.S.A.). Weighted population-based frequencies and prevalences were assessed for each survey (PROC SURVEYFREQ). Bivariate and multivariate survey logistic regression models were constructed for individual surveys and pooled years of NSCH or NHIS that accounted for the surveys' complex weighting. To better estimate the pooled prevalence of childhood ADD/ADHD among all 19 surveys, meta-analysis of the individual weighted multivariate regression analysis effects was performed using a robust variance estimation method,[19] as sample weights could not be combined due to differences in sampling methodology between NSCH and NHIS. The dependent variable in each model was the lifetime history of ADD/ADHD or current use of medication for ADD/ADHD. The independent variables were either 1-year history of eczema (yes/no) or eczema severity (none/mild/moderate/severe). Multivariate models included sex (M/F), age (2–5/6–11/12–17 years); race/ethnicity (white/black/Hispanic/multiracial or other); highest level of family education (less than high school/high school or 'general educational development'/more than high school); household income [0–99%/100–199%/200–399%/≥ 400% of the federal poverty level (FPL)]; birthplace (inside/outside the U.S.A), insurance status, lifetime history of asthma, 1-year history of hay fever and digestive allergy (all yes/no). Previous analyses have shown that child and adult patients with AD utilize significantly more healthcare than individuals without AD.[18,20,21] Thus, we created an additional multivariate model that also adjusted for number of outpatient healthcare visits in the past 12 months (0/1/2–3/4–9/10–12/13+ visits). Adjusted prevalence odds ratios (aOR) and 95% confidence intervals (CIs) were determined. Two-way interactions between

covariates were assessed and included in the models if significant ($P < 0{\cdot}01$) and modified the effect size by ≥ 20%.

Our *a priori* hypothesis was that: (i) severity and sleep disturbance act in concert to increase the risk of ADD/ADHD and that the presence of certain comorbidities, namely obesity, headaches and anaemia occurring in child patients with AD further increases the odds of ADD/ADHD; (ii) AD independent of other allergic disease is significantly associated with ADD/ADHD; (iii) AD is more strongly associated with severe compared with mild or moderate ADD/ADHD; and (iv) adult AD is also associated with ADHD and that similar comorbidities increase the risk of ADHD in patients with AD. History of childhood ADD/ADHD, AD, asthma, hay fever and food allergy were assessed in all surveys. Adult AD and ADD/ADHD were assessed in NHIS 2012. The number of nights of adequate sleep per week was assessed in NSCH 2003/4 and 2007/8 for children aged ≥ 6 years. AD and ADD/ADHD severity were assessed in NSCH 2007/8. Childhood AD and AD severity variables and interaction terms with nights of adequate sleep were included in multivariate models. Estimates of effect size for significant interactions between the two variables were determined for each level of the covariates using contrast statements. Questions utilized in this study are presented in Supplementary Table S2 (see Supporting Information). Complete data analysis was performed, i.e. subjects with missing data were excluded. The frequencies of missing values are presented in Supplementary Table S3 (see Supporting Information). Two-sided *P*-values < 0·05 were considered significant.

Results

Prevalence of atopic dermatitis and attention deficit (hyperactivity) disorder

Data were analysed for 354 416 U.S. children and adolescents aged 2–17 years, including those of all racial/ethnic groups, sex, levels of household income and birthplace. The pooled prevalence of AD from all 19 surveys was 10·1% (95% CI, 10·0–10·2%). The sociodemographic associations of paediatric AD have been previously described.[22]

The U.S. pooled prevalence of ADD/ADHD was found to be 7·3% (7·2–7·4%) in children. In bivariate logistic regression models, ADD/ADHD was associated with older age, lower household income, high school or ‘general educational development’ as highest level of household education (Supplementary Table S4; see Supporting Information). ADD/ADHD was inversely associated with female sex, Black/African-American and multiracial race, and Hispanic ethnicity, foreign birthplace and lack of insurance coverage.

In NHIS 2012, 4·2% (3·9–4·6%) of adults aged 18+ years reported a history of ADD/ADHD. The prevalence of adult AD in this sample was previously reported to be 7·2%.[1]

Association between atopic dermatitis and attention deficit (hyperactivity) disorder

The pooled U.S. prevalence of ADD/ADHD was 9·4% (9·1–·9·7%) in children with AD and 7·1% (7·0–7·2%) in children without AD (Table 1). In pooled multivariate analysis by a robust variance estimation method, childhood AD was associated with significantly higher odds of ADD/ADHD [aOR (95% CI), 1·14 (1·03–1·26)] in models adjusting for sociodemographics, comorbid allergic disease and healthcare utilization. In the NHIS 2012,

adult AD was also associated with significantly higher odds of ADD/ADHD [1·61 (1·25–2·06)] in a multivariate model adjusting for sociodemographics, allergic disease and healthcare utilization.

By caregiver report of medication usage (reported in the NSCH 2007/8), only 79·4% (95% CI: 77·2–81·7%) of children with ADD/ADHD were currently using any medications for ADD/ADHD. In multivariate models controlling for sociodemographics and comorbid allergic disease, AD was associated with significantly higher odds of currently using medication for ADD/ADHD [aOR (95% CI): 1·68 (1·30–·2·16)].

Association between attention deficit hyperactivity disorder and one or multiple allergic diseases

In multivariate models adjusting for sociodemographics and healthcare utilization, children with AD only [1·30 (1·22–·1·38)], asthma only [1·41 (1·34–1·48)], hay fever only [1·13 (1·08–1·19)], AD and asthma only [1·68 (1·49–1·89)], AD and hay fever [1·33 (1·21–1·45)], asthma and hay fever [1·38 (1·30–1·46)], and AD, asthma and hay fever [1·61 (1·47–1·76)] all had higher odds of ADD/ADHD (Table 2).

Association between atopic dermatitis, sleep disturbance and attention deficit (hyperactivity) disorder

In the NSCH 2003/4 and 2007/8, there was a significant two-way interaction between AD and severity of AD and the number of nights of adequate sleep as predictors of ADD/ADHD ($P < 0·0001$ for both). In unadjusted models, children without AD who had only 0–3 nights of adequate sleep [1·97 (1·71–2·26)] and those with AD who had 4–7 nights of adequate sleep [1·52 (1·32–1·75)] had significantly higher odds of ADD/ADHD (Table 3). However, children with both AD and only 0–3 nights of adequate sleep per week had even higher odds of ADD/ADHD [3·42 (2·55–4·57)]. These associations remained significant in multivariate analyses.

Children with severe AD (assessed in NSCH 2007/8) and only 0–3 nights of adequate sleep per week had dramatically higher odds of ADD/ADHD [34·90 (15·01–82·24)] than mild–moderate AD with 4–7 [1·61 (1·29–2·00)] or 0–3 [3·31 (2·28–4·79)] nights of adequate sleep per week or severe disease with 4–7 nights of adequate sleep per week [3·44 (2·00–5·93)] (Table 4). These associations remained significant in multivariate models. Similar trends were found in models of current use of medication for ADD/ADHD.

Association between atopic dermatitis and severity of attention deficit (hyperactivity) disorder in the National Survey of Children's Health 2007/8

The NSCH 2007/8 assessed caregiver-reported ADD/ADHD severity. In bivariate models, both mild [1·40 (1·09–1·80)] and moderate [1·59 (1·18–2·13)] ADD/ADHD were associated with higher odds of AD. However, severe ADD/ADHD was associated with the highest odds of AD [3·23 (2·13–·4·90)]. These associations remained significant in multivariate models (Supplementary Table S5; see Supporting Information).

Association between atopic dermatitis, comorbid health disorders and attention deficit (hyperactivity) disorder in children

Children with AD and comorbid anaemia [1·84 (1·37–2·46)], headaches [1·66 (1·49–1·85)] and obesity [1·28 (1·08–1·50)] had higher odds of ADD/ADHD in multivariate models adjusting for sociodemographics (Table 5).

Association between atopic dermatitis, comorbid health disorders and attention deficit (hyperactivity) disorder in adults

Among adults with AD, history of asthma [aOR (95% CI): 2·63 (1·58–4·37)] and food allergy [3·07 (1·64–5·77)], but not hay fever [1·57 (0·88–2·81)], were associated with higher odds of ADD/ADHD in multivariate models adjusting for sociodemographics (Table 6). Moreover, having one [2·29 (1·43–3·66)] or two or more additional [4·91 (2·43–9·93)] allergic diseases was associated with even higher odds of ADD/ADHD compared with children with AD and no additional allergic disease. Adults with AD and comorbid headaches [2·10 (1·17–3·75)] and insomnia [2·18 (1·28–3·71)], but not obesity [1·66 (0·96–2·87)], had higher odds of ADD/ADHD in multivariate models adjusting for sociodemographics. Interestingly, underweight body mass index (BMI) in adults with AD was associated with lower odds of ADD/ADHD [0·18 (0·03–0·96)].

Discussion

In an analysis of 19 U.S. population-based surveys, the present study found that AD is associated with increased odds of ADD/ADHD in children and adults, and increased odds of current use of medications for ADD/ADHD in children. Additionally, in analysis of pooled data, it was found that AD, asthma and hay fever, when unaccompanied by other allergic diseases, were each associated with increased odds of ADD/ADHD, although the association of hay fever was modest. Children with asthma and AD in combination had further increased odds of ADD/ADHD. These associations remained significant even after controlling for sociodemographics and healthcare utilization. In NSCH 2003/4 and 2007/8, it was found that children with AD and sleep disturbance have much higher odds of ADD/ADHD than children with either condition alone. Importantly though, children with AD alone or sleep disturbance alone also had increased risk of ADD/ADHD compared with children without either condition. In NSCH 2007/8, which assessed for AD severity, it was found that severe ADD/ADHD acted in a synergistic manner with sleep disturbance to substantially increase the risk of ADD/ADHD in children. Moreover, children with AD who had anaemia, headaches and obesity had even higher odds of ADD/ADHD than those with AD alone. Finally, adults with AD who had comorbid allergic disorders, insomnia and headaches had further increased risk of ADD/ADHD, and underweight BMI was protective against ADD/ADHD in adults with AD. Together, these results suggest that individuals with AD *per se* have higher odds of ADD/ADHD, although the presence of certain comorbidities confers even higher odds of ADD/ADHD.

The higher rates of being diagnosed with ADD/ADHD in AD raises some important questions. Firstly, do all these individuals actually have ADD/ADHD? It is likely that at least a subset actually have ADD/ADHD. However, some may simply have symptoms of AD that

resemble those of ADD/ADHD, such as difficulty with attention and concentration secondary to chronic itch and sleep loss. Moreover, a recent study found that toddlers with AD were more energetic and impulsive than healthy controls.[23] Thus, it is possible that improved treatment for AD might improve many of the symptoms of and obviate the need for treating ADD/ADHD. The design of the present study did not allow for us to elucidate these possibilities. Future prospective studies are needed to determine whether optimizing the treatment of childhood AD decreases the diagnosis and treatment of ADD/ADHD.

Importantly, there was a significant decrease in the ORs when outpatient healthcare visitation was added to the multivariate models, such that the overall adjusted, pooled OR for the relationship between AD and ADHD was just above significance [1·14 (1·03–1·26)]. This indicates that healthcare utilization is an important confounder in the relationship between AD and ADHD. Children with AD or ADHD are more likely to visit healthcare providers, which increases the likelihood that comorbid conditions are diagnosed. Given these results, future analyses of the relationship between AD and ADHD should include adjustments for healthcare utilization.

This study confirms previous studies that found associations between childhood AD and ADD/ADHD,[2–9] and that sleep disturbance and disease severity may modify the relationship. One previous meta-analysis of four studies found a 43% increased risk of ADHD diagnosis or ADHD symptoms in children with AD,[8] comparable with the 46% increased risk in our pooled meta-analysis. Another cross-sectional study examined 13 318 children aged 3–17 years in Germany and found that AD was associated with higher odds of ADHD. In a subgroup analysis of children aged 3–11 years, sleeping problems was found to be an effect modifier in that there was a strong association between AD and ADHD in children with sleeping problems, but no significant association in children without sleeping problems.[12] In contrast, the present study found that although children with sleep disturbance and AD have the highest odds of ADD/ADHD, children with AD and no sleep disturbance also have increased odds of ADD/ADHD. Another previous study examined data from the NSCH 2007/8 and found that eczema was associated with ADHD in a group of children aged 2–5 years, and that these children were at higher risk for injury requiring medical attention.[9] Yaghmaie *et al.*[6] previously examined AD severity data in the NSCH 2007/8 and found that severe AD was most strongly associated with ADHD. Furthermore, they found that there was an interaction between AD and 0–7 nights of adequate sleep per week on the risk of ADHD in multivariate models adjusting for sociodemographics, 0–7 adequate nights of sleep, smoking in the household and history of asthma.[6] Our analyses build on these previous findings by demonstrating that severe AD and sleep disturbance independently and synergistically contribute to an increased risk of ADHD. Further, this increased risk remained significant even after controlling for healthcare utilization. Notably, though, sleep disturbance has also been associated with ADHD,[24] independent of the presence of AD, and thus, it is possible that sleep disturbance in ADHD predisposes a child towards AD. Using the present study design, we could not determine if sleep disturbance was due to itch and AD, or rather due to ADHD. Future studies could help determine this.

One previous analysis examined the relationship between each atopic disease and ADHD, while controlling for additional atopic disease, and found that AD, allergic rhinitis and

asthma in males but not females, were significantly associated with ADHD.[3] Additionally, they found that the risk of ADHD increases with increasing number of comorbid allergic diseases. In contrast, our present study found that AD alone, asthma alone, and hay fever alone are each significantly associated with ADHD, and that the combination of eczema and asthma further increases the ADHD risk. Our findings indicate that there is perhaps a multifactorial aetiology of increased ADHD risk in AD, where itch, sleep and predisposition to atopy each contribute. Previous studies have found differing results on whether or not hay fever is truly associated with ADHD.[5,25]

To our knowledge, the relationship between ADD/ADHD severity and AD found in the present study has not been previously demonstrated. The reasons for these findings are still unclear. It is possible that children with severe AD have more severe symptoms of itch, causing them to exhibit more severe symptoms of inattention and hyperactivity. Conversely, it is also possible that children with ADD/ADHD, particularly children with severe ADD/ADHD, are more likely to scratch, resulting in exacerbation of skin symptoms. Further prospective studies with objective determination of severity of ADD/ADHD and AD could help to elucidate the reasons for these findings.

Our study also found that headaches, obesity and anaemia occurring in children with AD further increase the risk of ADD/ADHD. Anaemia, obesity and headaches have previously been associated with ADHD and hyperactive-impulsive behavior. [26–29] To our knowledge, there are no previous epidemiological or prospective analyses that have evaluated any interplay between AD and obesity, anaemia or headaches and risk of ADD/ADHD in children.

We found a significant relationship between adult AD and history of ADD/ADHD, after controlling for sociodemographics, comorbid allergic disease and healthcare utilization. Additionally, asthma, food allergy, headaches, insomnia and multiple comorbid allergic diseases, but not hay fever or obesity, in adults with AD further increase the risk of ADD/ADHD, although underweight BMI appears to be protective. Previous studies of the relationship between AD and ADHD have been limited to analyses of children and adolescents, even though AD often persists into adulthood.[30] Adults with AD and ADD/ADHD likely developed their ADD/ADHD during childhood. However, history of ADD/ADHD may be an indicator of more severe AD that persists into adulthood. Future studies of adult populations are needed to confirm these findings, and to determine the underlying reasons why certain adults with AD are at higher risk of ADHD.

The mechanism by which AD confers increased odds of ADD/ADHD remains unknown. Prospective studies have demonstrated a temporal relationship in which AD precedes the diagnosis of ADD/ADHD,[2] suggesting a priming effect of AD to subsequent development of ADD/ADHD. Previous studies speculate on multiple mechanisms by which AD might upregulate neuroimmune factors, e.g. neuropeptide-induced sensitivity[31] and inflammatory cytokines, resulting in heightened sensitivity to stimuli,[32,33] poor sleep and the subsequent development of ADD/ADHD.[34,35] Sleep disturbance in AD might be related to chronic itch, inflammation[36,37] and degree of atopy.[38] In turn, these sleep disturbances may unmask

symptoms of inattention and hyperactivity.[39] The relationship between AD, sleep disturbance and ADD/ADHD requires further exploration.

The present study has numerous strengths including the use of 19 U.S. population-based surveys of children, each with rigorous methodology and a large sample size, incorporating children of all ages, races/ethnicities and socioeconomic statuses. The results demonstrate a highly reproducible association between AD and ADD/ADHD. Additionally, the use of multivariate logistic regression models allowed for the control of many confounding sociodemographic variables, history of comorbid allergic disease and healthcare utilization. However, this study is not without weakness. Although we were able to control for a number of variables in our models, we are not able to rule out the possibility of residual confounding, which is important given the modest pooled association between AD and ADD/ADHD. ADD/ADHD history was determined by caregiver report of physician diagnosis in the NSCH and caregiver report in the NHIS and not verified by a physician, and as a result of the question wording, we were not able to distinguish between ADD and ADHD, and the association between AD and each separate disorder may be different. Caregiver-reported and self-reported ADD/ADHD diagnosis has not been validated by a prospective study against a clinical standard. However, a previous study found evidence of convergent validity between the prevalence of childhood ADHD as reported by caregivers and the prevalence of ADHD as determined by medical record.[40,41] Further, it is possible that reported current use of medications for ADD/ADHD may be an even more accurate measure of ADD/ADHD than caregiver report as medications would require a physician diagnosis. Parental report of ADHD medication usage has not been validated against a clinical standard, although one previous study has validated dispensed ADHD medications with physician diagnosis.[42] Additionally, the prevalence of adult ADHD of 4·2% determined by the present study is comparable with the prevalence of 4·4% found by a previous study, which was determined by clinician assessment.[43] Nevertheless, ADHD is primarily a disease of childhood onset and thus may be affected by misclassification and recall bias, particularly in the adult sample. AD history was similarly determined by caregiver report of physician diagnosis in the NSCH and caregiver report in NHIS and not verified by a physician. Previous studies found good concordance between self-reported AD and AD diagnosed by medical examination.[44,45] Moreover, we recently performed a multicentre study to validate the question employed in the NSCH and found the question to have a sensitivity and specificity of 0·70 and 0·96, respectively, for AD.[46] Importantly, the specificity of the question is high, indicating that positive respondents very likely have AD. However, there is some concern for misclassification of patients with AD who respond negatively to the question. The result of this is that our determined ORs are likely slightly lower than they would be if there was no misclassification. We ultimately believe that the case definition for AD is sufficiently valid for epidemiological study. The question that assessed food allergy was unspecific, inquiring about ‘digestive allergy’ and not verified by physician or allergist evaluation. The likely effect of this question wording is that the reported food allergy prevalence is higher than the true prevalence in this population. Finally, the cross-sectional design of our study prevents any conclusions from being made on direction of association, causality or temporality. Perhaps there are unknown genetic or environmental factors that are responsible for both increased risk of sleep disturbance and ADD/ADHD in certain patients

with AD. Future prospective studies with objective determination of ADD/ADHD and AD severity could provide further information on precise aetiology, and could discern any effect that AD treatment or therapeutic control has on risk of ADD/ADHD.

The findings of this study are consistent with previous studies that demonstrate an increased risk of ADHD in children with AD. Additionally, the present study demonstrates that adult AD is associated with increased risk of ADHD – a finding that begs replication in future studies. Additionally, our study found that AD, unaccompanied by other allergic disease, is associated with increased ADHD risk. Further, the findings of this study confirm and expand on previous studies that have found sleep disturbance, disease severity and comorbid allergic disease as factors that further increase ADHD risk in children. The present study also found that AD is most strongly associated with severe ADHD, and that obesity, anaemia and headaches increase the risk of ADHD in children with AD. Finally, asthma, headaches and insomnia increase the risk of ADHD in adults, while underweight BMI may be protective. Further, prospective studies are needed to determine the reasons for these findings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Silverberg JI, Garg NK, Paller AS, et al. Sleep disturbances in adults with eczema are associated with impaired overall health: a US population-based study. J Invest Dermatol. 2015; 135:56–66. [PubMed: 25078665]
2. Genuneit J, Braig S, Brandt S, et al. Infant atopic eczema and subsequent attention-deficit/hyperactivity disorder – a prospective birth cohort study. Pediatr Allergy Immunol. 2014; 25:51–6. [PubMed: 24289041]
3. Tsai JD, Chang SN, Mou CH, et al. Association between atopic diseases and attention-deficit/hyperactivity disorder in childhood: a population-based case–control study. Ann Epidemiol. 2013; 23:185–8. [PubMed: 23375343]
4. Schmitt J, Romanos M, Schmitt NM, et al. Atopic eczema and attention- deficit/hyperactivity disorder in a population-based sample of children and adolescents. JAMA. 2009; 301:724–6. [PubMed: 19224748]
5. Schmitt J, Buske-Kirschbaum A, Roessner V. Is atopic disease a risk factor for attention-deficit/hyperactivity disorder? A systematic review Allergy. 2010; 65:1506–24. [PubMed: 20716320]
6. Yaghmaie P, Koudelka CW, Simpson EL. Mental health comorbidity in patients with atopic dermatitis. J Allergy Clin Immunol. 2013; 131:428–33. [PubMed: 23245818]
7. Chen MH, Su TP, Chen YS, et al. Attention deficit hyperactivity disorder, tic disorder, and allergy: is there a link? A nationwide population- based study. J Child Psychol Psychiatry. 2013; 54:545–51. [PubMed: 23140273]
8. Schmitt J, Apfelbacher C, Heinrich J, et al. Association of atopic eczema and attention-deficit/hyperactivity disorder – meta-analysis of epidemiologic studies. Z Kinder Jugendpsychiatr Psychother. 2013; 41:35–42. Article in German. [PubMed: 23258436]

9. Garg N, Silverberg JI. Association between childhood allergic disease, psychological comorbidity, and injury requiring medical attention. Ann Allergy Asthma Immunol. 2014; 112:525–32. [PubMed: 24713577]
10. Schmitt J, Apfelbacher C, Chen CM, et al. Infant-onset eczema in relation to mental health problems at age 10 years: results from a prospective birth cohort study (German Infant Nutrition Intervention plus). J Allergy Clin Immunol. 2010; 125:404–10. [PubMed: 20159252]
11. Schmitt J, Chen CM, Apfelbacher C, et al. Infant eczema, infant sleeping problems, and mental health at 10 years of age: the prospective birth cohort study LISAplus. Allergy. 2011; 66:404–11. [PubMed: 21029113]
12. Romanos M, Gerlach M, Warnke A, et al. Association of attention-deficit/hyperactivity disorder and atopic eczema modified by sleep disturbance in a large population-based sample. J Epidemiol Community Health. 2010; 64:269–73. [PubMed: 19692717]
13. Silverberg JI, Kleiman E, Lev-Tov H, et al. Association between obesity and atopic dermatitis in childhood: a case–control study. J Allergy Clin Immunol. 2011; 127:1180–6. e1. [PubMed: 21411132]
14. Silverberg JI, Simpson EL. Association between obesity and eczema prevalence, severity and poorer health in US adolescents. Dermatitis. 2014; 25:172–81. [PubMed: 25000233]
15. Silverberg JI, Becker L, Kwasny M, et al. Central obesity and high blood pressure in pediatric patients with atopic dermatitis. JAMA Dermatol. 2015; 151:144–52. [PubMed: 25536049]
16. Drury KE, Schaeffer M, Silverberg JI. Association between atopic disease and anemia in US children. JAMA Pediatr. 2016; 170:29–34. [PubMed: 26619045]
17. Silverberg JI. Association between childhood eczema and headaches: an analysis of 19 US population-based studies. J Allergy Clin Immunol. 2016; 137(492–9):e5.
18. Silverberg JI, Simpson EL. Association between severe eczema in children and multiple comorbid conditions and increased healthcare utilization. Pediatr Allergy Immunol. 2013; 24:476–86. [PubMed: 23773154]
19. Hedges LV, Tipton E, Johnson MC. Robust variance estimation in meta-regression with dependent effect size estimates. Res Synth Methods. 2010; 1:39–65. [PubMed: 26056092]
20. Strom MA, Silverberg JI. Utilization of preventive health care in adults and children with eczema. Am J Prev Med. 2016; 50:e33–44. [PubMed: 26547540]
21. Silverberg JI. Health care utilization, patient costs, and access to care in US adults with eczema: a population-based study. JAMA Dermatol. 2015; 151:743–52. [PubMed: 25738422]
22. Silverberg JI, Paller AS. Association between eczema and stature in 9 US population-based studies. JAMA Dermatol. 2015; 151:401–9. [PubMed: 25493447]
23. Sedighipour L, Firooz A, Pourpak Z, et al. Behavioral characteristics in 18- to 36-month-old toddlers with atopic dermatitis compared with healthy children. Pediatr Dermatol. 2010; 27:314–15. [PubMed: 20609162]
24. Cortese S, Faraone SV, Konofal E, et al. Sleep in children with attention- deficit/hyperactivity disorder: meta-analysis of subjective and objective studies. J Am Acad Child Adolesc Psychiatry. 2009; 48:894–908. [PubMed: 19625983]
25. Tsai MC, Lin HK, Lin CH, et al. Prevalence of attention deficit/hyperactivity disorder in pediatric allergic rhinitis: a nationwide population- based study. Allergy Asthma Proc. 2011; 32:41–6. [PubMed: 22221429]
26. Konofal E, Lecendreux M, Arnulf I, et al. Iron deficiency in children with attention-deficit/hyperactivity disorder. Arch Pediatr Adolesc Med. 2004; 158:1113–15. [PubMed: 15583094]
27. Cortese S, Moreira-Maia CR, St Fleur D, et al. Association between ADHD and obesity: a systematic review and meta-analysis. Am J Psychiatry. 2016; 173:34–43. [PubMed: 26315982]
28. Arruda MA, Guidetti V, Galli F, et al. Migraine, tension-type headache, and attention-deficit/hyperactivity disorder in childhood: a population-based study. Postgrad Med. 2010; 122:18–26. [PubMed: 20861584]
29. Fasmer OB, Halmoy A, Oedegaard KJ, et al. Adult attention deficit hyperactivity disorder is associated with migraine headaches. Eur Arch Psychiatry Clin Neurosci. 2011; 261:595–602. [PubMed: 21394551]

30. Margolis JS, Abuabara K, Bilker W, et al. Persistence of mild to moderate atopic dermatitis. JAMA Dermatol. 2014; 150:593–600. [PubMed: 24696036]
31. Labrecque G, Vanier MC. Biological rhythms in pain and in the effects of opioid analgesics. Pharmacol Ther. 1995; 68:129–47. [PubMed: 8604435]
32. Shani-Adir A, Rozenman D, Kessel A, et al. The relationship between sensory hypersensitivity and sleep quality of children with atopic dermatitis. Pediatr Dermatol. 2009; 26:143–9. [PubMed: 19419459]
33. Engel-Yeger B, Mimouni D, Rozenman D, et al. Sensory processing patterns of adults with atopic dermatitis. J Eur Acad Dermatol Venereol. 2011; 25:152–6. [PubMed: 20561126]
34. Buske-Kirschbaum A, Schmitt J, Plessow F, et al. Psychoendocrine and psychoneuroimmunological mechanisms in the comorbidity of atopic eczema and attention deficit/hyperactivity disorder. Psychoneuroendocrinology. 2013; 38:12–23. [PubMed: 23141851]
35. Suárez AL, Feramisco JD, Koo J, Steinhoff M. Psychoneuroimmunology of psychological stress and atopic dermatitis: pathophysiologic and therapeutic updates. Acta Derm Venereol. 2012; 92:7–15. [PubMed: 22101513]
36. Bender BG, Ballard R, Canono B, et al. Disease severity, scratching, and sleep quality in patients with atopic dermatitis. J Am Acad Dermatol. 2008; 58:415–20. [PubMed: 18280338]
37. Leo HL, Bender BG, Leung SB, et al. Effect of pimecrolimus cream 1% on skin condition and sleep disturbance in children with atopic dermatitis. J Allergy Clin Immunol. 2004; 114:691–3. [PubMed: 15446293]
38. Chang YS, Chou YT, Lee JH, et al. Atopic dermatitis, melatonin, and sleep disturbance. Pediatrics. 2014; 134:e397–405. [PubMed: 25022734]
39. Dahl RE, Bernhisel-Broadbent J, Scanlon-Holdford S, et al. Sleep disturbances in children with atopic dermatitis. Arch Pediatr Adolesc Med. 1995; 149:856–60. [PubMed: 7633537]
40. Visser SN, Danielson ML, Bitsko RH, et al. Convergent validity of parent-reported attention-deficit/hyperactivity disorder diagnosis: a cross-study comparison. JAMA Pediatr. 2013; 167:674–5. [PubMed: 23700143]
41. Getahun D, Jacobsen SJ, Fassett MJ, et al. Recent trends in childhood attention-deficit/hyperactivity disorder. JAMA Pediatr. 2013; 167:282–8. [PubMed: 23338799]
42. Giacobini M, Medin E, Ahnemark E, et al. Prevalence, patient characteristics, and pharmacological treatment of children, adolescents, and adults diagnosed with ADHD in Sweden. J Atten Disord. 2014; doi: 10.1177/1087054714554617
43. Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry. 2006; 163:716–23. [PubMed: 16585449]
44. Susitaival P, Husman L, Hollmén A, Horsmanheimo M. Dermatoses determined in a population of farmers in a questionnaire-based clinical study including methodology validation. Scand J Work Environ Health. 1995; 21:30–5.
45. Flohr C, Weinmayr G, Weiland SK, et al. How well do questionnaires perform compared with physical examination in detecting flexural eczema? Findings from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Two. Br J Dermatol. 2009; 161:846–53. [PubMed: 19485999]
46. Silverberg JI, Patel N, Immaneni S, et al. Assessment of atopic dermatitis using self- and caregiver-report: a multicenter validation study. Br J Dermatol. 2015; 173:1400–4. [PubMed: 26186170]

What's already known about this topic?

- Childhood atopic dermatitis (AD) is associated with increased risk of attention deficit hyperactivity disorder (ADHD); sleep disturbance and disease severity have been implicated as modifying factors.

What does this study add?

- Severe AD and sleep disturbance independently and synergistically contribute to increased risk of ADHD.
- AD unaccompanied by other allergic diseases is associated with increased risk of attention deficit disorder (ADD)/ADHD.
- Obesity, headaches and anaemia further increase the risk of ADD/ADHD in children with AD.
- Adult AD is associated with increased risk of ADHD. Asthma, headaches and insomnia increase the risk of ADHD in adult patients with AD, and underweight body mass index is protective.

Table 1

Association between eczema and ADD/ADHD in children, adolescents and adults

	ADD/ADHD				
Study	**Total subjects**	**% Prev (95% CI)**	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**	**Adjusted OR 2 (95% CI)**
Pooled NHIS (children)[a]					
No eczema	163 522	6·4 (6·2–6·5)	1 (ref)	1 (ref)	1 (ref)
Eczema	17 277	9·1 (8·7–9·5)	**1·46 (1·36–1·57)**	**1·35 (1·24–1·46)**	**1·11 (1·01–1·21)**
Pooled NSCH (children)[b]					
No eczema	152 934	7·8 (7·7–8·0)	1 (ref)	1 (ref)	1 (ref)
Eczema	18 588	9·6 (9·2–10·0)	**1·45 (1·28–1·63)**	**1·48 (1·29–1·70)**	**1·25 (1·08–1·45)**
Pooled NHIS and NSCH (children)[c]					
No eczema	316 456	7·1 (7·0–7·2)	1 (ref)	1 (ref)	1 (ref)
Eczema	35 865	9·4 (9·1–9·7)	**1·46 (1·36–1·57)**	**1·36 (1·22–1·49)**	**1·14 (1·03–1·26)**
NHIS 2012 (adults aged 18+ years)					
No eczema	32 072	4·0 (3·7–4·3)	1 (ref)	1 (ref)	1 (ref)
Eczema	2483	7·5 (5·9–9·1)	**1·94 (1·52–2·48)**	**1·73 (1·35–2·22)**	**1·61 (1·25–2·06)**

Binary logistic regression models were constructed with ADHD as the dependent variable and eczema as the independent variable. Multivariate logistic regression models were then constructed that included eczema, sex, age, race, household income, highest level of household education, U.S. vs. foreign birthplace, insurance coverage, lifetime history of asthma, and 1-year history of hay fever and food allergy as the independent variables. A second multivariate model was created that additionally controlled for healthcare utilization in the past year. Adjusted prevalence ORs and 95% CIs were estimated. ADD/ADHD, attention deficit (hyperactivity) disorder; CI, confidence interval; NHIS, National Health Interview Survey; NSCH, National Survey of Children's Health; OR, odds ratio; prev, prevalence; ref, reference; **bold** indicates significance.

[a] Pooled analyses were performed by merging the datasets and dividing NHIS sample weights by the number of studies ($n = 17$).

[b] Pooled analyses were performed by merging the datasets and dividing NSCH sample weights by the number of studies ($n = 2$).

[c] Due to differences in sampling methodology between NHIS and NSCH, sample weights could not be combined. Meta-analyses of multivariate regression analysis effects were performed using a robust variance estimation method.

Table 2

Association between allergic disease and attention deficit (hyperactivity) disorder (ADD/ADHD) in U.S. children and adolescents (n = 354 416)

	ADD/ADHD					
	No (n = 32 504)	Yes (n = 173)				
Allergic disease	**Freq**	**Freq**	**% Prev (95% CI)**	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**	**Adjusted OR 2 (95% CI)**
None	225 654	14 492	6·0 (5·9–6·1)	1·00 (ref)	1·00 (ref)	1·00 (ref)
Eczema only	17 813	1402	7·3 (6·9–7·7)	**1·23 (1·16–1·30)**	**1·41 (1·33–1·50)**	**1·30 (1·22–1·38)**
Asthma only	21 461	2630	10·9 (10·5–11·3)	**1·91 (1·83–1·99)**	**1·58 (1·50–1·66)**	**1·41 (1·34–1·48)**
Hay fever only	32 389	3177	8·9 (8·6–9·2)	**1·53 (1·47–1·59)**	**1·28 (1·22–1·34)**	**1·13 (1·08–1·19)**
Eczema and asthma	3117	420	11·9 (10·8–12·9)	**2·10 (1·89–2·33)**	**2·06 (1·84–2·31)**	**1·68 (1·49–1·89)**
Eczema and hay fever	6629	717	9·8 (9·1–10·4)	**1·68 (1·56–1·82)**	**1·65 (1·51–1·80)**	**1·33 (1·21–1·45)**
Asthma and hay fever	13 521	1995	12·9 (12·3–13·4)	**2·30 (2·19–2·42)**	**1·75 (1·66–1·85)**	**1·38 (1·30–1·46)**
Eczema, asthma and hay fever	4741	805	14·5 (13·6–15·4)	**2·65 (2·45–2·86)**	**2·32 (2·13–2·53)**	**1·61 (1·47–1·76)**

Binary, unweighted logistic regression models were constructed with ADHD as the dependent variable and allergic disease as the independent variable. Multivariate logistic regression models were then constructed that included eczema, sex, age, race, household income, highest level of household education, U.S. vs. foreign birthplace and insurance coverage as the independent variables. A second multivariate model was created that additionally controlled for healthcare utilization in the past year. Adjusted prevalence ORs and 95% CIs were estimated. CI, confidence interval; freq, frequency; OR, odds ratio; prev, prevalence; **bold** indicates significance.

Table 3

Association between paediatric eczema, sleep and ADD/ADHD in NSCH 2003/4 and 2007/8

		ADD/ADHD					
		No (*n* = 119 361)	Yes (*n* = 13 341)				
Eczema	**Nights of adequate sleep**	**Freq**	**Freq**	**Prev (95% CI)**	**OR (95% CI)**	**Adj OR (95% CI)**	**Adj OR 2 (95% CI)**
No	4–7	98 399	9940	8·7 (8·4–9·1)	1·00 (ref)	1·00 (ref)	1·00 (ref)
No	0–3	8508	1555	15·8 (14·0–17·6)	**1·97 (1·71–2·26)**	**1·80 (1·54–2·09)**	**1·78 (1·51–2·09)**
Yes	4–7	10 191	1385	12·7 (11·2–14·1)	**1·52 (1·32–1·75)**	**1·44 (1·23–1·68)**	**1·32 (1·12–1·56)**
Yes	0–3	1074	288	24·6 (19·2–29·9)	**3·42 (2·55–4·57)**	**3·16 (2·30–4·35)**	**2·82 (2·05–3·86)**

Binary, survey-weighted logistic regression models were constructed with ever history of ADHD as the dependent variables and the interaction of eczema and adequate nights of sleep per week (0–3/4–7) as the independent variables. Crude prevalence ORs and 95% CIs were estimated. Multivariate models additionally included age, sex, race/ethnicity, household income, highest level of parental education, insurance coverage, U.S. or foreign birthplace and lifetime history of asthma, hay fever and food allergy as categorical variables. The second multivariate model additionally included healthcare utilization as an independent variable. ADD/ADHD, attention deficit (hyperactivity) disorder; CI, confidence interval; freq, frequency; NSCH, National Survey of Children's Health; OR, odds ratio; prev, prevalence; **bold** indicates significance.

Table 4

Association between eczema severity, sleep and ADHD in the National Survey of Children's Health 2007/8

		History of ADD/ADHD					
		No (n = 74 527)	Yes (n = 7252)				
						Adjusted OR (95% CI)	
Eczema	**Nights of adequate sleep**	**Freq**	**Freq**	**% Prev (95% CI)**	**Crude OR (95% CI)**	**Model-1**	**Model-2**
No	4–7	46 299	5027	9·9 (9·7–10·2)	1·00 (ref)	1·00 (ref)	1·00 (ref)
	0–3	4122	859	17·2 (16·2–18·3)	**2·31 (1·86–2·87)**	**1·37 (1·24–1·52)**	**1·83 (1·47–2·26)**
Mild–moderate	4–7	5095	696	12·0 (11·2–12·9)	**1·61 (1·29–2·00)**	**1·59 (1·25–2·03)**	**1·56 (1·22–1·99)**
	0–3	514	151	22·7 (19·5–25·9)	**3·31 (2·28–4·79)**	**3·12 (2·02–4·83)**	**2·90 (1·87–4·52)**
Severe	4–7	274	86	23·9 (11·9–33·5)	**3·44 (2·00–5·93)**	**3·01 (1·73–5·26)**	**3·05 (1·62–5·74)**
	0–3	41	35	46·1 (34·8–57·3)	**34·90 (15·01–82·24)**	**25·52 (11·27–57·77)**	**16·83 (7·02–40·33)**
	Current use of medication for ADD/ADHD						
		No (n = 65 081)	Yes (n = 4982)				
Mild–moderate	4–7	4654	496	11·3 (9·1–13·4)	**1·53 (1·21–1·94)**	**1·48 (1·10–1·99)**	**1·49 (1·25–2·11)**
	0–3	483	103	16·2 (11·0–21·4)	**2·34 (1·58–3·46)**	**1·47 (0·88–2·46)**	**2·35 (1·40–3·95)**
Severe	4–7	254	72	22·6 (13·7–31·5)	**3·53 (2·11–5·92)**	**3·41 (1·82–6·40)**	**3·93 (1·70–9·10)**
	0–3	35	24	59·2 (30·4–88·0)	**17·49 (5·29–57·78)**	**21·67 (5·26–89·34)**	**12·42 (4·13–20·10)**

Binary, survey-weighted logistic regression models were constructed with ever history of ADD/ADHD and current use of medications for ADD/ADHD as the binary dependent (outcome) variables and history or severity of eczema, average nights of adequate sleep per week in the past year and a statistical interaction term between them as the independent variables. Prevalence ORs and 95% CIs were determined. The interaction term between severe eczema and 0–3 nights of adequate sleep was significant (P < 0·0001). Two different multivariate models were constructed. Model-1 included age, sex, race/ethnicity, household income, highest level of parental education, insurance coverage, U.S. or foreign birthplace and lifetime history of asthma, hay fever and food allergy as categorical variables. Model-2 additionally included healthcare utilization as an independent variable. ADD/ADHD, attention deficit (hyperactivity) disorder; CI, confidence interval; freq, frequency; OR, odds ratio; prev, prevalence; **bold** indicates significance.

Table 5

Association between allergic disease, anaemia, adiposity and ADD/ADHD in children with eczema (n = 35 865)

	ADD/ADHD				
	No (n = 32 504)	Yes (n = 3361)			
Variable	**Freq**	**Freq**	**% Prev (95% CI)**	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**
Anaemia					
No	15 291	1505	9·0 (8·5–9·4)	1·00 (ref)	1·00 (ref)
Yes	384	68	15·0 (11·7–18·3)	**1·80 (1·38–2·34)**	**1·84 (1·37–2·46)**
Headaches					
No	24 893	2646	9·6 (9·3–10·0)	1·00 (ref)	1·00 (ref)
Yes	2656	626	19·0 (17·7–20·4)	**2·22 (2·02–2·44)**	**1·66 (1·49–1·85)**
Body mass index (percentile)					
< 5	356	77	17·8 (14·2–21·4)	**1·38 (1·07–1·78)**	1·20 (0·87–1·64)
5–84	5591	878	13·6 (12·7–14·4)	1·00 (ref) 1·00 (ref)	
85–94	1560	277	15·1 (13·4–16·7)	1·13 (0·98–1·31)	1·10 (0·92–1·30)
≥ 95	1485	366	19·8 (18·0–21·6)	**1·57 (1·37–1·80)**	**1·28 (1·08–1·50)**

Binary, unweighted logistic regression models were constructed with ADD/ADHD as the dependent variable and history of allergic disease, anaemia and body mass index for age and sex percentiles as the independent variables. Analyses were limited to subjects with a history of eczema. Multivariate logistic regression models were then constructed that included sex, age, race, household income, highest level of household education, U.S. vs. foreign birthplace and insurance coverage as the independent variables. Crude and adjusted prevalence ORs and 95% CIs were estimated. ADD/ADHD, attention deficit (hyperactivity) disorder; CI, confidence interval; freq, frequency; OR, odds ratio; prev, prevalence; **bold** indicates significance.

Table 6

Association between allergic disease, headaches, insomnia, adiposity and attention deficit (hyperactivity) disorder (ADD/ADHD) in adults with eczema (*n* = 2488)

	ADD/ADHD				
	No (*n* = 32 504)	Yes (*n* = 173)			
Variable	**Freq**	**Freq**	**% Prev (95% CI)**	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**
Ever asthma					
No	1756	96	5·3 (4·0–6·7)	1·00 (ref)	1·00 (ref)
Yes	552	77	13·8 (9·1–18·5)	**2·83 (1·76–4·55)**	**2·63 (1·58–4·37)**
Hay fever					
No	1986	141	7·2 (5·5–8·9)	1·00 (ref)	1·00 (ref)
Yes	322	32	9·3 (5·2–13·3)	1·32 (0·76–2·28)	1·57 (0·88–2·81)
Food allergy					
No	2000	133	6·3 (4·9–7·6)	1·00 (ref)	1·00 (ref)
Yes	305	40	15·6 (7·8–23·3)	**2·77 (1·47–5·20)**	**3·07 (1·64–5·77)**
Headaches					
No	1738	107	6·0 (4·5–7·4)	1·00 (ref)	1·00 (ref)
Yes	571	66	12·0 (7·5–16·4)	**2·14 (1·30–3·52)**	**2·10 (1·17–3·75)**
Insomnia					
No	1497	80	5·7 (3·7–7·7)	1·00 (ref)	1·00 (ref)
Yes	813	93	10·9 (8·2–13·5)	**2·01 (1·27–3·19)**	**2·18 (1·28–3·71)**
Number of allergic disorders					
0	1423	64	4·6 (3·2–6·0)	1·00 (ref)	1·00 (ref)
1	627	74	9·7 (6·9–12·4)	**2·22 (1·42–3·58)**	**2·29 (1·43–3·66)**
2 or more	251	35	17·8 (8·8–26·8)	**4·49 (2·25–8·96)**	**4·91 (2·43–9·93)**
Body mass index class					
Underweight	45	4	2·4 (0·0–4·9)	0·32 (0·10–1·01)	**0·18 (0·03–0·96)**
Normal weight	754	60	7·1 (4·9–9·2)	1·00 (ref)	1·00 (ref)
Overweight	696	47	6·7 (4·2–9·3)	0·95 (0·56–1·61)	1·06 (0·62–1·81)
Obese	723	58	9·6 (5·9–13·4)	1·40 (0·81–2·41)	1·66 (0·96–2·87)

Binary, weighted logistic regression models were constructed with ADD/ADHD as the dependent variable and history of allergic disease, headaches, insomnia and body mass index class as the independent variables. Analyses were limited to subjects with a history of eczema. Multivariate logistic regression models were then constructed that included sex, age, race, household income, highest level of

household education, U.S. vs. foreign birthplace and insurance coverage as the independent variables. Crude and adjusted prevalence ORs and 95% CIs were estimated. CI, confidence interval; freq, frequency; OR, odds ratio; prev, prevalence; **bold** indicates significance.