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Asthma, hay fever, and food allergy are associated with caregiver-reported speech disorders in US children

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Abstract

Background—Children with asthma, hay fever, and food allergy may have several factors that increase their risk of speech disorder, including allergic inflammation, ADD/ADHD, and sleep disturbance. However, few studies have examined a relationship between asthma, allergic disease, and speech disorder. We sought to determine whether asthma, hay fever, and food allergy are associated with speech disorder in children and whether disease severity, sleep disturbance, or ADD/ADHD modified such associations.

Methods—We analyzed cross-sectional data on 337,285 children aged 2–17 years from 19 US population-based studies, including the 1997–2013 National Health Interview Survey and the 2003/4 and 2007/8 National Survey of Children's Health.

Results—In multivariate models, controlling for age, demographic factors, healthcare utilization, and history of eczema, lifetime history of asthma (odds ratio [95% confidence interval]: 1.18 [1.04–1.34], p = 0.01), and one-year history of hay fever (1.44 [1.28–1.62], p < 0.0001) and food allergy (1.35 [1.13–1.62], p = 0.001) were associated with increased odds of speech disorder. Children with current (1.37 [1.15–1.59] p = 0.0003) but not past (p = 0.06) asthma had increased risk of speech disorder. In one study that assessed caregiver-reported asthma severity, mild (1.58 [1.20–2.08], p = 0.001) and moderate (2.99 [1.54–3.41], p < 0.0001) asthma were associated with increased odds of speech disorder; however, severe asthma was associated with the highest odds of speech disorder (5.70 [2.36–13.78], p = 0.0001).

Conclusion—Childhood asthma, hay fever, and food allergy are associated with increased risk of speech disorder. Future prospective studies are needed to characterize the associations.

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Supporting Information
Additional Supporting Information may be found in the online version of this article

Keywords

asthma; hay fever; food allergy; speech disorder; speech delay; allergy; atopic disease; ADD/ ADHD; sleep disturbance

Allergic diseases such as asthma, hay fever, and food allergy are common childhood inflammatory disorders with considerable impact on the lives of those affected (1). Children with allergic disease utilize substantial healthcare services and incur significant medical expenses compared to children with no disease (2–4). Additionally, allergic diseases are associated with decreased quality of life (1, 5), increased risk of psychological disorders (6), and numerous medical and non-medical comorbidities.

Childhood speech and language disorders are a heterogeneous group of conditions with varying developmental consequences. Primary speech and language impairment affects between 2 and 7% of children (7). We recently reported on the association between eczema and speech disorder in US children (8). We hypothesized that such association was related to the effects of chronic disease during childhood development and chronic sleep deprivation. Similarly, childhood asthma and allergic rhinitis are associated with sleep disturbance (9, 10), allergic inflammation (11, 12), and Attention Deficit Disorder/Attention Deficit Hyperactivity Disorder (ADD/ADHD) (13, 14), which may affect neurocircuitry involved in speech and language and increase the risk of childhood speech disorders (15–17). Food allergy may increase the risk of speech disorder through allergic inflammation and a possible, though controversial, link to chronic otitis media (18, 19). Several small studies found abnormalities in vocal quality and articulation in children with chronic asthma and allergic rhinitis, potentially related to inhaled corticosteroids (20–23). However, an epidemiologic study found no significantly increased prevalence of asthma and allergy in children with speech disorder (24). Our a *priori* hypothesis was that childhood asthma, hay fever, and food allergy are associated with increased risk of speech disorder. Additionally, we hypothesized that severe allergic disease and allergic disease accompanied by sleep disturbance or ADD/ ADHD were associated with even higher risk of speech disorder. This study sought to determine whether there is an association between childhood allergic disease and speech disorders.

Methods

Study sources

After approval from the institutional review board at Northwestern University, cross-sectional data from 19 different population-based studies, including the 1997–2013 National Health Interview Survey (NHIS) and the 2003/4 and 2007/8 National Survey of Children's Health (NSCH), were assessed. The specific characteristics of each survey are presented in Table S1. Briefly, both the NHIS, collected in-person by trained interviewers, and NSCH, collected over telephone, were surveys designed and overseen by the National Center for Health Statistics (NCHS), for the purpose of estimating the prevalence of health issues affecting children in the United States. In households that were selected to participate in NHIS or NSCH, one child was randomly chosen to be the subject of an interview with the caregiver, and each study year included a sample of subjects drawn independently from previous years. Inherent to each survey's design is a complex, multistage probability sample that incorporated demographic data from the U.S. Census bureau. From this incorporated data, the NCHS created sample weights that allow for prevalence estimations that are representative of the US population of non-institutionalized children. In this study, prevalence estimates of data from either NHIS or NSCH reflect this complex weighting process. However, in pooled prevalence estimates of data from all 19 surveys, sample weights could not be combined due to differences in sampling methodology between the two survey vehicles.

Outcomes

The questions used in this study are presented in Table S2. Associations between speech disorder and lifetime history of asthma, one-year history of hay fever, and food allergy were assessed in all 19 surveys. Asthma history was stratified into current vs. past asthma, and association with speech disorders was assessed in 15 surveys. NSCH 2007/8 assessed for caregiver-reported severity of allergic disease and speech disorder. NSCH 2003/4 and 2007/8 assessed for ADD/ADHD and adequate nights of sleep per week. Finally, the association between asthma, hay fever, food allergy, and speech disorder, as modified by sleep disturbance, defined by less than 4 nights of adequate sleep per week, or ADD/ADHD, was assessed by testing two-way interaction terms.

Statistical analysis

Data analyses were performed using SAS version 9.4. (SAS Institute, Cary, North Carolina) SURVEY procedures were utilized to estimate prevalence and construct logistic regression models that accounted for the complex survey weighting. Bivariate associations were examined with history of speech disorder as the dependent variable and asthma, asthma severity, hay fever, or food allergy as the independent variables. We were concerned that sociodemographic factors, rates of outpatient healthcare utilization, and comorbidity with eczema (8) might be confounders in the association of asthma with speech disorder. Multivariate models included history of eczema (Y/N), sex (male/female), age (2–6/7–11/12–17), race/ethnicity (Hispanic/ non-Hispanic white/non-Hispanic black/multiracial or other), household income (0–99%/100–199%/200–399%/400% Federal Poverty Level [FPL]), highest level of household/parental education (less than high school [HS]/HS or equivalent/more than HS), birthplace in the US (Y/N), insurance coverage (Y/N), and outpatient healthcare utilization over the past year (0/1/2–3/ 4–9/10–12/13+ visits) as additional independent variables. In logistic regression models of pooled data from either NHIS or NSCH, sample weights were combined due to similar sampling methodologies between survey years. Due to differences in methodology between NHIS and NSCH, sample weights could not be combined. Thus, pooled analyses were assessed by performing meta-analysis of individual survey effects using a robust variance estimation method (25). Odds ratios (OR) and 95% confidence ratios (CI) were determined. Complete data analysis was performed. The frequency of missing values is presented in Table S3.

Results

The prevalence and demographics of childhood speech disorders in the examined studies have been described previously (8). Briefly, the pooled prevalence of speech disorder in US children was 2.4% and speech disorder was positively associated with male sex, younger age, and lower socioeconomic status.

Allergy and speech disorder

In bivariate models of data pooled from NHIS 1997–2013, NSCH 2003/4 & 2007/8, and in meta-analysis, lifetime asthma, one-year history of hay fever, and food allergy were all associated with increased odds of speech disorder ($p < 0.0001$ for all). Multivariate modeling of data pooled from NHIS 1997 to 2013 found lifetime asthma (aOR [95% CI]: 1.18 [1.04–1.34], $p = 0.01$), one-year history of hay fever (1.44 [1.28–1.62], $p < 0.0001$), and one-year history of food allergy (1.35 [1.13–1.62], $p = 0.001$) to be associated with increased odds of speech disorder (Table 1). Multivariate modeling of data pooled from NSCH found lifetime asthma (1.55 [1.33–1.82], $p < 0.0001$), one-year history of hay fever (1.51 [1.30–1.74], $p < 0.0001$), and food allergy (2.30 [1.78–2.98], $p < 0.0001$) to be associated with increased odds of speech disorder. In meta-analysis of the multivariate model effects from all 19 studies, lifetime asthma (1.23 [1.12–1.35], $p < 0.0001$), hay fever (1.51 [1.31–1.71], $p < 0.0001$), and food allergy (1.44 [1.19–1.70], $p = 0.0002$) were associated with increased odds of speech disorder. No interactions were found between allergic disease and age, indicating the associations occurred at all ages throughout childhood.

Current and past asthma and speech disorder

In bivariate models of data pooled from NHIS 2001 to 2013, current (2.15 [1.88–2.46], $p < 0.0001$) but not past (1.24 [0.99–1.57], $p = 0.07$) asthma was associated with increased odds of speech disorder (Table 1). These associations remained significant in multivariate models. Similar results were found in data pooled from NSCH. In meta-analysis of bivariate model effects from all 15 individual studies, current (2.20 [1.96–2.44], $p < 0.0001$) but not past ($p = 0.06$) asthma were associated with increased odds of speech disorder. Meta-analysis of individual multivariate model effects found current (1.37 [1.15–1.59], $p = 0.0003$) but not past ($p = 0.95$) asthma to be associated with increased risk of speech disorder.

Severity of allergy and speech disorder

Mild (1.99 [1.56–2.55], $p < 0.0001$) and moderate (3.93 [2.60–5.92], $p < 0.0001$) asthma were associated with increased odds of speech disorder. However, severe asthma was associated with dramatically higher odds of speech disorder (11.82 [5.79–24.12], $p < 0.0001$) in bivariate modeling (Table 2). All three associations remained significant in multivariate models.

Similarly, mild (1.50 [1.18–1.90], $p = 0.0009$), moderate (2.67 [2.02–3.53], $p < 0.0001$), and severe (3.44 [2.23–5.30], $p < 0.0001$) hay fever were associated with increased odds of speech disorder. The associations of mild and moderate hay fever remained significant in multivariate models.

Finally, mild (1.52 [1.09–2.11], p = 0.01), moderate (5.59 [3.32–9.39], p < 0.0001), and severe (3.33 [1.96–5.68]), p < 0.0001) food allergy were also significantly associated with increased risk of speech disorder. The associations of moderate and severe food allergy remained significant in multivariate models.

Allergy, sleep, and speech disorder

Children with either sleep disturbance (1.50 [1.16–1.94], p = 0.002) or current asthma (2.38 [1.83–2.92], p < 0.0001) had increased odds of speech disorder compared to children without either condition alone. However, even higher odds of speech disorder were found in children with both asthma and sleep disturbance (3.10 [1.93–5.01], p < 0.0001) (Table 3). This pattern was consistent in multivariate models. Similar results were found in bivariate and multivariate models of hay fever or food allergy and sleep disturbance (Table 3).

Allergy, ADD/ADHD, and speech disorder

Moreover, ADD/ADHD alone (3.83 [3.28–4.47], p < 0.0001) or current asthma alone (2.21 [1.86–2.53], p < 0.0001) were both associated with increased odds of speech disorder in bivariate modeling. However, children with both ADD/ADHD and current asthma had the highest odds of speech disorder (8.00 [6.03–10.61], p < 0.0001). This pattern was consistent in multivariate models, and similar results were found in bivariate and multivariate models of hay fever or food allergy and ADD/ ADHD disturbance (Table 4).

Severity of speech disorder and allergy

Children with current asthma compared to those without asthma had significantly higher odds of mild (3.33 [2.45–4.52], p < 0.0001), moderate (2.19 [1.47–3.26], p = 0.0001), and severe (2.51 [1.57–4.01], p = 0.0001) speech disorder in bivariate models (Table S4). The association between mild (2.37 [1.72–3.26], p < 0.0001) and moderate (1.55 [1.05–2.30], p = 0.03) but not severe speech disorder (p = 0.14) remained significant in multivariate models. Hay fever and food allergy were both significantly associated with mild, moderate, and severe speech disorder in bivariate and multivariate models (p < 0.05 for all) (Table S4).

Discussion

The present study found that current history of asthma and one-year history of hay fever and food allergy were significantly associated with increased risk of speech disorder. In a single study that assessed caregiver-reported allergic disease severity, a dose–response effect was determined with severe asthma having a much stronger association with speech disorder than mild or moderate disease, although this dose–response pattern did not hold for hay fever and food allergy. Finally, asthma, hay fever, and food allergy in combination with sleep disturbance or ADD/ADHD were associated with increased risk of speech disorder than any allergy alone.

The characteristics of speech disorder in children with asthma, hay fever, and food allergy have not been fully elucidated. A previous epidemiologic analysis reported on the associations of childhood speech disorder, using data from the 1995 Australian Health Survey on 12,388 children aged 0–14 years, and found the prevalence of childhood speech disorder to be 1.7% (24). This was comparable to the pooled prevalence of 2.4% in the samples analyzed by the present study. However, although the previous study increased prevalence of asthma and allergy in children with speech disorder, the difference was not significant (24). Another study evaluated measures of vocal quality in 40 adults with asthma and 40 age- and sex-matched controls via subjective self-assessment, clinician evaluation, acoustic analyses, and videolaryngostroboscopy (22). Using both self-assessment and clinician assessment, significantly more asthmatics were found to have abnormalities in vocal quality compared to controls. Using videolaryngostroboscopy, patients with asthma were found to have significantly higher rates of at least one abnormality (97.5%) compared with controls (40%). Other studies evaluated the correlation between inhaled corticosteroids and voice disturbances in asthmatics, although these studies did not examine speech patterns or language mastery. A small study found that speech therapy resulted in earlier and longer-lasting control of asthma and allergic rhinitis symptoms in mouth-breathing children (26). Notably, none of these studies controlled for disease severity, medical comorbidity, or sleep disturbance on the association between asthma or hay fever and speech disorder.

The mechanisms of association of childhood asthma and hay fever with speech disorder are likely multifactorial, including the effects of chronic allergic inflammation and sleep disturbance. Asthma and hay fever are associated with immunologic aberrancy including IgE hypersecretion and a Th2 cytokine profile (11, 12). These inflammatory cytokines may cross the blood–brain barrier (27) and affect behavioral, executive, and emotional neurocircuitry. Indeed, a previous functional magnetic resonance imaging study of individuals undergoing asthma episodes found increased activation of the anterior cingulate cortex (ACC) (28), a portion of the brain active during normal speech (29). Abnormal activation of the ACC has also been demonstrated during silent reading and speech tasks in individuals who stutter (30). It is possible that repeated inflammatory insults to neurocircuitry relevant to speech and language increase risk of speech disorders in children with allergy. Similar mechanisms have been posited for the relationship between allergy and ADHD (13, 31). Sleep disturbance may impact language development in childhood (15, 16). One study compared the early-life sleep patterns of 1029 sets of twins from the Quebec Newborn Twin study using assessments of expressive and receptive vocabulary. Children with more consolidated sleep at 6 and 18 months of age had better language skills at ages 18, 30, and 60 months, suggesting that sleep consolidation may have a causal effect on language development (16). Another study found that short sleep duration was associated with a threefold higher risk of poor performance on standardized language assessment, indicating a role for adequate sleep in language acquisition (15). Thus, sleep disturbance in asthma and hay fever may negatively impact on language development. Indeed, the present study found that children with asthma or hay fever and sleep disturbance had the highest odds of speech disorder. However, even children with asthma or hay fever and no sleep disturbance had higher odds of speech disorder compared to children without allergic disease. Future, prospective studies could help determine the etiology of speech disorder in children with asthma and hay fever.

Our study also found a significant association between food allergy and speech disorder, with an effect size similar to the association of asthma and speech disorder. This association may be related to increased allergic inflammation (32) similarly to asthma and hay fever, or due to a link between childhood food allergy and chronic otitis media (18, 19). To our knowledge, there are no previous epidemiologic or prospective analyses that have evaluated any interplay between food allergy and speech disorder. Future, prospective and laboratory studies are needed to illuminate the reasons for these findings.

The present study has several strengths, including the use of 19 population-based studies, each with a large sample size and minimal selection bias, allowing for the assessment of asthma, hay fever, food allergy, and speech disorder in children of all ages and demographic backgrounds. Furthermore, the use of multivariate logistic regression models allowed for the control for potentially confounding variables. The association between allergic disease and speech disorder was highly reproducible and consistent between each study. However, there are several limitations. Asthma, hay fever, and food allergy history were determined by caregiver report and not verified by physician evaluation. Past validation studies have generally found good concordance of asthma and hay fever self-report and that determined by clinician evaluation (33, 34). Speech disorder was also determined by caregiver report and not confirmed by physician or speech pathologist. As such, we were unable to determine what patterns of speech disorder are associated with asthma, hay fever, and food allergy. The questions assessing speech disorder between NSCH and NHIS were slightly different, with NSCH assessing for ‘stuttering, stammering, and other speech problems’ and NHIS assessing for only ‘stuttering or stammering’. This difference might be responsible for possible heterogeneity among respondents of the different surveys. The cross-sectional design prevents any conclusions from being made on causality or direction of association. It is possible that asthma somehow interferes with language development impacting speech disorder. It is also possible that there are unknown genetic or environmental factors that influence both the development of asthma or allergic disease and speech disorder. Finally, we were unable to determine whether treatments for asthma, hay fever, or sleep disturbance could affect manifestation of speech disorder or vice versa. One previous case report found subjective improvement in vocal quality of a patient with asthma after undergoing allergen immunotherapy (35). A small study found that patients with allergic rhinitis or asthma who had undergone allergen immunotherapy for more than 2 years had a significantly lower prevalence of vocal symptoms than those who had not (36). Given these findings and the theorized impact that inflammation may have on speech-related neurocircuitry, it may be that early control of asthma or allergic inflammation mitigates the development of speech disorder. Future experimental and prospective clinical studies with precise determination of speech disorder and allergic disease could help provide this knowledge.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

aOR	adjusted odds ratio
CI	confidence interval
FPL	Federal Poverty Level
GED	general educational development
NCHS	National Center for Health Statistics
NHIS	National Health Interview Survey
NSCH	National Survey of Children's Health
OR	odds ratio
Prev	prevalence

References

1. O'Connell EJ. The burden of atopy and asthma in children. Allergy. 2004; 59(Suppl 78):7–11. [PubMed: 15245350]
2. Branum AM, Lukacs SL. Food allergy among children in the United States. Pediatrics. 2009; 124:1549–55. [PubMed: 19917585]
3. Lozano P, Fishman P, VonKorff M, Hecht J. Health care utilization and cost among children with asthma who were enrolled in a health maintenance organization. Pediatrics. 1997; 99:757–64. [PubMed: 9164766]
4. Bhattacharyya N. Incremental healthcare utilization and expenditures for allergic rhinitis in the United States. Laryngoscope. 2011; 121:1830–3. [PubMed: 21997726]
5. Cummings AJ, Knibb RC, King RM, Lucas JS. The psychosocial impact of food allergy and food hypersensitivity in children, adolescents and their families: a review. Allergy. 2010; 65:933–45. [PubMed: 20180792]
6. Garg N, Silverberg JI. Association between childhood allergic disease, psychological comorbidity, and injury requiring medical attention. Annals of allergy, asthma & immunology: official publication of the American College of Allergy, Asthma, & Immunology. 2014; 112:525–32.
7. Law J, Boyle J, Harris F, Harkness A, Nye C. Prevalence and natural history of primary speech and language delay: findings from a systematic review of the literature. Int J Lang Commun Disord. 2000; 35:165–88. [PubMed: 10912250]
8. Strom MA, Silverberg JI. Eczema Is associated with childhood speech disorder: a retrospective analysis from the National Survey of Children's Health and the National Health Interview Survey. J Pediatr. 2016; 168(185–92):e4.
9. Craig TJ, McCann JL, Gurevich F, Davies MJ. The correlation between allergic rhinitis and sleep disturbance. J Allergy Clin Immunol. 2004; 114:S139–45. [PubMed: 15536445]
10. Mastronarde JG, Wise RA, Shade DM, Olopade CO, Scharf SM. American lung association asthma clinical research C. Sleep quality in asthma: results of a large prospective clinical trial. J Asthma. 2008; 45:183–9. [PubMed: 18415823]
11. Barnes PJ. Th2 cytokines and asthma: an introduction. Respir Res. 2001; 2:64–5. [PubMed: 11686866]
12. Pawankar RU, Okuda M, Suzuki K, Okumura K, Ra C. Phenotypic and molecular characteristics of nasal mucosal gamma delta T cells in allergic and infectious rhinitis. Am J Respir Crit Care Med. 1996; 153:1655–65. [PubMed: 8630617]

13. 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]
14. Chou PH, Lin CC, Lin CH, el Loh W, Chan CH, Lan TH. Prevalence of allergic rhinitis in patients with attention-deficit/hyperactivity disorder: a population-based study. Eur Child Adolesc Psychiatry. 2013; 22:301–7. [PubMed: 23274480]
15. Touchette E, Petit D, Seguin JR, Boivin M, Tremblay RE, Montplaisir JY. Associations between sleep duration patterns and behavioral/cognitive functioning at school entry. Sleep. 2007; 30:1213–9. [PubMed: 17910393]
16. Dionne G, Touchette E, Forget-Dubois N, et al. Associations between sleep-wake consolidation and language development in early childhood: a longitudinal twin study. Sleep. 2011; 34:987–95. [PubMed: 21804661]
17. Sciberras E, Mueller KL, Efron D, et al. Language problems in children with ADHD: a community-based study. Pediatrics. 2014; 133:793–800. [PubMed: 24753530]
18. Holm VA, Kunze LH. Effect of chronic otitis media on language and speech development. Pediatrics. 1969; 43:833–9. [PubMed: 5769509]
19. Teele DW, Klein JO, Rosner BA. Otitis media with effusion during the first three years of life and development of speech and language. Pediatrics. 1984; 74:282–7. [PubMed: 6540437]
20. Williamson IJ, Matusiewicz SP, Brown PH, Greening AP, Crompton GK. Frequency of voice problems and cough in patients using pressurized aerosol inhaled steroid preparations. Eur Respir J. 1995; 8:590–2. [PubMed: 7664859]
21. Ihre E, Zetterstrom O, Ihre E, Hammarberg B. Voice problems as side effects of inhaled corticosteroids in asthma patients–a prevalence study. J Voice. 2004; 18:403–14. [PubMed: 15331115]
22. Dogan M, Eryuksel E, Kocak I, Celikel T, Sehitoglu MA. Subjective and objective evaluation of voice quality in patients with asthma. J Voice. 2007; 21:224–30. [PubMed: 16504474]
23. Baker BM, Baker CD, Le HT. Vocal quality, articulation and audiological characteristics of children and young adults with diagnosed allergies. Ann Otol Rhinol Laryngol. 1982; 91:277–80. [PubMed: 7092048]
24. Keating D, Turrell G, Ozanne A. Childhood speech disorders: reported prevalence, comorbidity and socioeconomic profile. J Paediatr Child Health. 2001; 37:431–6. [PubMed: 11885704]
25. Hedges LV, Tipton E, Johnson MC. Robust variance estimation in meta-regression with dependent effect size estimates. Research synthesis methods. 2010; 1:39–65. [PubMed: 26056092]
26. Campanha SM, Fontes MJ, Camargos PA, Freire LM. The impact of speech therapy on asthma and allergic rhinitis control in mouth breathing children and adolescents. J Pediatr (Rio J). 2010; 86:202–8. [PubMed: 20449526]
27. Banks WA, Kastin AJ, Broadwell RD. Passage of cytokines across the blood-brain barrier. NeuroImmunoModulation. 1995; 2:241–8. [PubMed: 8963753]
28. Rosenkranz MA, Busse WW, Johnstone T, et al. Neural circuitry underlying the interaction between emotion and asthma symptom exacerbation. Proc Natl Acad Sci U S A. 2005; 102:13319–24. [PubMed: 16141324]
29. Paus T, Petrides M, Evans AC, Meyer E. Role of the human anterior cingulate cortex in the control of oculomotor, manual, and speech responses: a positron emission tomography study. J Neurophysiol. 1993; 70:453–69. [PubMed: 8410148]
30. Craig-McQuaide A, Akram H, Zrinzo L, Tripoliti E. A review of brain circuitries involved in stuttering. Front Hum Neurosci. 2014; 8:884. [PubMed: 25452719]
31. Buske-Kirschbaum A, Schmitt J, Plessow F, Romanos M, Weidinger S, Roessner V. Psychoendocrine and psychoneuroimmunological mechanisms in the comorbidity of atopic eczema and attention deficit/hyperactivity disorder. Psychoneuroendocrinology. 2013; 38:12–23. [PubMed: 23141851]
32. Dang TD, Tang ML, Koplin JJ, et al. Characterization of plasma cytokines in an infant population cohort of challenge-proven food allergy. Allergy. 2013; 68:1233–40. [PubMed: 24033562]
33. Senthilselvan A, Dosman JA, Chen Y. Relationship between pulmonary test variables and asthma and wheezing: a validation of self-report of asthma. The Journal of asthma: official journal of the Association for the Care of Asthma. 1993; 30:185–93. [PubMed: 8325827]

34. Kilpelainen M, Terho EO, Helenius H, Koskenvuo M. Validation of a new questionnaire on asthma, allergic rhinitis, and conjunctivitis in young adults. Allergy. 2001; 56:377–84. [PubMed: 11350300]

35. Cohn JR, Sataloff RT, Branton C. Response of asthma-related voice dysfunction to allergen immunotherapy: a case report of confirmation by methacholine challenge. J Voice. 2001; 15:558–60. [PubMed: 11792032]

36. Simberg S, Sala E, Tuomainen J, Ronnemaa AM. Vocal symptoms and allergy–a pilot study. J Voice. 2009; 23:136–9. [PubMed: 17624725]

Table 1

Association between allergic disease and speech disorder in NHIS 1997–2013 and NSCH 2003/4 and 2007/8

		No speech disorder	Speech disorder					
Study	**Allergic disease**	**Freq**	**Freq**	**% Prev (95% CI)**	**Crude OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**	**p-value**
Pooled NHIS (1997–2013)	Lifetime asthma[†]							
	No	142,590	2212	1.5 (1.5–1.6)	1 [ref]	–	1 [ref]	–
	Yes	24,093	732	2.8 (2.6–3.1)	**1.86 (1.67–2.07)**	**<0.0001**	**1.18 (1.04–1.34)**	**0.01**
	Asthma status[§]							
	Never	104,611	1657	1.6 (1.5–1.7)	1 [ref]	–	1 [ref]	–
	Past, not current	5999	134	1.9 (1.5–2.4)	1.24 (0.99–1.57)	0.07	0.99 (0.76–1.29)	0.94
	Current	12,484	443	3.3 (2.9–3.7)	**2.15 (1.88–2.46)**	**<0.0001**	**1.28 (1.09–1.50)**	**0.002**
	Hay fever[†]							
	No	135,324	2065	1.5 (1.4–1.6)	1 [ref]	–	1 [ref]	–
	Yes	31,071	874	2.6 (2.4–2.8)	**1.75 (1.59–1.94)**	**<0.0001**	**1.44 (1.28–1.62)**	**<0.0001**
	Food allergy[†]							
	No	159,943	2672	1.6 (1.6–1.7)	1 [ref]	–	1 [ref]	–
	Yes	6733	271	3.3 (2.8–3.7)	**2.02 (1.74–2.36)**	**<0.0001**	**1.35 (1.13–1.62)**	**0.001**
Pooled NSCH	Lifetime asthma[‡]							
	No	139,860	4147	3.2 (3.0–3.4)	1 [ref]	–	1 [ref]	–
	Yes	21,854	1160	6.4 (5.6–7.1)	**2.07 (1.80–2.37)**	**<0.0001**	**1.55 (1.33–1.82)**	**<0.0001**
	Asthma status[¶]							
	Never	144,007	4147	3.2 (3.0–3.4)	1 [ref]	–	1 [ref]	–
	Past, not current	6615	220	3.8 (2.7–4.8)	1.19 (0.89–1.60)	0.24	1.07 (0.77–1.50)	0.94
	Current	15,239	940	7.5 (6.6–8.4)	**2.46 (2.12–2.85)**	**<0.0001**	**1.73 (1.46–2.06)**	**<0.0001**
	Hay fever[‡]							
	No	132,451	3813	3.2 (3.0–3.4)	1 [ref]	–	1 [ref]	–
	Yes	29,083	1496	5.7 (5.2–6.3)	**1.84 (1.63–2.08)**	**<0.0001**	**1.51 (1.30–1.74)**	**<0.0001**
	Food allergy[‡]							
	No	155,292	4766	3.4 (3.2–3.5)	1 [ref]	–	1 [ref]	–
	Yes	6435	545	10.5 (8.7–12.4)	**3.39 (2.76–4.17)**	**<0.0001**	**2.30 (1.78–2.98)**	**<0.0001**

Study	Allergic disease	No speech disorder	Speech disorder					
		Freq	Freq	% Prev (95% CI)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Pooled (all)	Lifetime asthma[††]							
	No	282,450	6359	2.2 (2.1–2.3)	1 [ref]	–	1 [ref]	–
	Yes	45,947	1892	4.0 (3.8–4.1)	**1.89 (1.73–2.05)**	**<0.0001**	**1.23 (1.12–1.35)**	**<0.0001**
	Asthma status[††]							
	Never	244,571	5804	2.3 (2.3–2.4)	1 [ref]	–	1 [ref]	–
	Past, not current	12,614	354	2.7 (2.4–3.0)	1.25 (0.95–1.55)	0.06	0.99 (0.77–1.21)	0.95
	Current	27,723	1383	4.8 (4.5–5.0)	**2.20 (1.96–2.44)**	**<0.0001**	**1.37 (1.15–1.59)**	**0.0003**
	Hay fever[††]							
	No	267,775	5878	2.1 (2.1–2.2)	1 [ref]	–	1 [ref]	–
	Yes	60,154	2370	3.8 (3.6–3.9)	**1.82 (1.58–2.05)**	**<0.0001**	**1.51 (1.31–1.71)**	**<0.0001**
	Food allergy[††]							
	No	315,235	7438	2.3 (2.3–2.4)	1 [ref]	–	1 [ref]	–
	Yes	13,168	816	5.8 (5.4–6.2)	**2.15 (1.82–2.47)**	**<0.0001**	**1.44 (1.19–1.70)**	**0.0002**

Binary logistic regression models were constructed with speech disorder as the dependent variable and hay fever, food allergy, lifetime history of asthma and asthma status (never, past, current) as the binary independent variables. Multivariate logistic regression models were then constructed that additionally included history of eczema, sex, age, race, household income, highest level of household education, US vs. foreign birthplace, insurance coverage, and outpatient healthcare utilization in the past year as the independent variables. Adjusted prevalence odds ratios and 95% confidence intervals were estimated.

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

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

[§]Pooled analyses were performed by merging the datasets and dividing NHIS sample weights by the number of studies (n = 13).

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

[††]Due to differences in sampling methodology between NHIS and NSCH, sample weights could not be combined. Unweighted prevalence estimates are presented. Pooled prevalence odds ratios were determined by meta-analysis of weighted multivariate regression analysis effects, using a robust variance estimation method. Bold values indicate P < 0.05.

Table 2

Association between allergic disease severity and speech disorder in NSCH 2007/8

	History of speech disorder						
	No (n = 77,196)	Yes (n = 2676)					
Allergic disease severity	Freq	Freq	% Prevalence	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Current asthma							
None	70,106	2177	3.3 (3.0–3.6)	1.00	–	1.00	–
Mild	5129	286	6.3 (5.0–7.7)	**1.99 (1.56–2.55)**	**<0.0001**	**1.58 (1.20–2.08)**	**0.001**
Moderate	1525	142	11.8 (7.6–15.9)	**3.93 (2.60–5.92)**	**<0.0001**	**2.29 (1.54–3.41)**	**<0.0001**
Severe	251	55	28.6 (14.2–43.1)	**11.82 (5.79–24.12)**	**<0.0001**	**5.70 (2.36–13.78)**	**0.0001**
Hay fever							
None	62,525	1893	3.3 (3.0–3.7)	1.00	–	1.00	–
Mild	10,239	453	4.9 (3.9–5.9)	**1.50 (1.18–1.90)**	**0.0009**	**1.39 (1.07–1.79)**	**0.01**
Moderate	3762	257	8.4 (6.4–10.4)	**2.67 (2.02–3.53)**	**<0.0001**	**2.08 (1.46–2.97)**	**<0.0001**
Severe	474	65	10.6 (6.6–14.6)	**3.44 (2.23–5.30)**	**<0.0001**	1.54 (0.90–2.66)	0.12
Food allergy							
None	73,563	2370	3.5 (3.2–3.8)	1.00	–	1.00	–
Mild	1782	124	5.3 (3.7–6.8)	**1.52 (1.09–2.11)**	**0.01**	1.21 (0.83–1.75)	0.32
Moderate	992	102	16.9 (9.7–24.1)	**5.59 (3.32–9.39)**	**<0.0001**	**3.48 (1.97–6.16)**	**<0.0001**
Severe	738	71	10.9 (5.8–15.9)	**3.33 (1.96–5.68)**	**<0.0001**	**2.02 (1.03–3.97)**	**0.04**

Binary logistic regression models were constructed with history of speech disorder as the binary dependent variable. The independent (explanatory) variable was severity of asthma, hay fever, or food/digestive allergy (mild/moderate/severe). Prevalence odds ratios (OR) and 95% confidence intervals (95% CI) were determined. Multivariate logistic regression models were created that included allergic disease severity, history of eczema, age, gender, race/ethnicity, Hispanic origin, household income, birthplace in the United States, highest level of education in the household, insurance coverage, and outpatient healthcare utilization in the past year (all categorical) as independent variables. Adjusted prevalence odds ratios (aOR) and 95% confidence intervals (95% CI) were determined. Bold values indicate $P < 0.05$.

Table 3

Association between allergic disease, adequate nights of sleep per week, and speech disorder in NSCH 2003/4 and 2007/8

		History of speech disorder						
		No (n = 128,075)	Yes (n = 3555)					
	Nights of adequate sleep per week	Freq	Freq	% Prevalence	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Current asthma								
No	4–7	105,686	2632	2.7 (2.5–2.9)	1.00	–	1.00	–
No	0–3	9652	296	3.9 (3.0–4.8)	**1.50 (1.16–1.94)**	**0.002**	**1.76 (1.32–2.34)**	**0.0001**
Yes	4–7	11,025	541	6.1 (5.0–7.2)	**2.38 (1.93–2.92)**	**<0.0001**	**1.56 (1.22–1.983)**	**0.0003**
Yes	0–3	2049	112	7.8 (4.4–11.2)	**3.10 (1.92–5.01)**	**<0.0001**	**2.51 (1.64–3.88)**	**<0.0001**
Hay fever								
No	4–7	95,000	2275	2.7 (2.5–2.9)	1.00	–	1.00	–
No	0–3	8492	243	4.0 (2.9–5.1)	**1.52 (1.13–2.04)**	**0.005**	**1.81 (1.33–2.48)**	**0.0002**
Yes	4–7	21,862	902	4.4 (3.9–4.9)	**1.67 (1.43–1.94)**	**<0.0001**	**1.29 (1.09–1.53)**	**0.003**
Yes	0–3	2579	135	6.0 (4.3–7.7)	**2.32 (1.70–3.18)**	**<0.0001**	**2.06 (1.46–2.91)**	**<0.0001**
Food allergy								
No	4–7	112,700	2881	2.8 (2.6–3.0)	1.00	–	1.00	–
No	0–3	10,541	328	4.1 (3.1–5.0)	**1.50 (1.16–1.92)**	**0.002**	**1.76 (1.35–2.29)**	**<0.0001**
Yes	4–7	4280	296	9.3 (6.9–11.6)	**3.60 (2.69–4.81)**	**<0.0001**	**2.35 (1.61–3.43)**	**<0.0001**
Yes	0–3	545	49	12.1 (6.7–17.6)	**4.88 (2.92–8.14)**	**<0.0001**	**3.80 (2.13–6.79)**	**<0.0001**

Binary logistic regression models were constructed with history of speech disorder as the dependent variable and the interaction between current asthma, hay fever, or food allergy and nights of adequate sleep per week (0–3/4–7) as the independent variable. Multivariate models were also constructed that additionally included history of eczema, sex, age, race, household income, highest level of household education, US vs. foreign birthplace, insurance coverage, and outpatient healthcare utilization in the past year (all categorical) as independent variables. Adjusted prevalence odds ratios and 95% confidence intervals were estimated. Bold values indicate $P < 0.05$.

Table 4

Association between allergic disease, ADD/ADHD, and speech disorder in NSCH 2003/4 and 2007/8

		History of speech disorder						
		No (n = 161,934)	Yes (n = 5329)					
	ADD/ADHD	Freq	Freq	% Prevalence	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Current asthma								
No	No	135,527	3377	2.7 (2.5–2.9)	1.00	–	1.00	–
No	Yes	10,597	948	9.6 (6.4–10.8)	**3.83 (3.28–4.47)**	**<0.0001**	**3.88 (3.25–4.63)**	**<0.0001**
Yes	No	12,892	621	5.8 (4.9–6.6)	**2.21 (1.86–2.63)**	**<0.0001**	**1.71 (1.40–2.09)**	**<0.0001**
Yes	Yes	1885	281	18.1 (14.0–22.1)	**8.00 (6.03–10.61)**	**<0.0001**	**6.29 (4.53–8.73)**	**<0.0001**
Hay fever								
No	No	122,640	2943	2.7 (2.5–2.8)	1.00	–	1.00	–
No	Yes	9499	831	10.0 (8.6–11.4)	**4.07 (3.43–4.83)**	**<0.0001**	**4.12 (3.38–5.02)**	**<0.0001**
Yes	No	25,987	1074	4.6 (4.1–5.1)	**1.77 (1.54–2.03)**	**<0.0001**	**1.59 (1.35–1.88)**	**<0.0001**
Yes	Yes	3013	401	14.2 (11.6–16.8)	**6.07 (4.86–7.59)**	**<0.0001**	**5.35 (4.11–6.96)**	**<0.0001**
Food allergy								
No	No	143,061	3628	2.8 (2.6–2.9)	1.00	–	1.00	–
No	Yes	11,857	1090	10.1 (8.9–11.2)	**3.94 (3.42–4.54)**	**<0.0001**	**3.83 (3.26–4.51)**	**<0.0001**
Yes	No	5746	389	8.3 (6.6–9.9)	**3.17 (2.53–3.99)**	**<0.0001**	**2.15 (1.64–2.81)**	**<0.0001**
Yes	Yes	666	143	25.8 (17.3–34.3)	**12.18 (7.77–19.10)**	**<0.0001**	**9.11 (4.92–16.88)**	**<0.0001**

Binary logistic regression models were constructed with history of speech disorder as the dependent variable and the interaction between current asthma, hay fever, or food allergy and ADD/ADHD (Y/N) as the independent variable. Multivariate models were also constructed that additionally included history of eczema, sex, age, race, household income, highest level of household education, US vs. foreign birthplace, insurance coverage, and outpatient healthcare utilization in the past year (all categorical) as independent variables. Adjusted prevalence odds ratios and 95% confidence intervals were estimated. Bold values indicate $P < 0.05$.