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Atopic Dermatitis Independently Increases Sensitization above Parental Atopy: the MPAACH Study

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Capsule Summary

Early sensitization is ~50% higher in children with atopic dermatitis compared to children from a high-risk allergy cohort with comparable rates of parental atopy. AD may increase sensitization risk over heredity alone.

Keywords

sensitization; atopic dermatitis; pediatric; high-risk; cohort

To the Editor:

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Birth cohort studies have yielded important information regarding sensitization profiles in early life and their associations with the development of subsequent allergic disease. The design of these cohorts differs and these differences are critical to the interpretation of the data. Higher rates of sensitization have been established in high-risk cohorts of children who have a family history of allergies and asthma compared to unselected population cohorts. Indeed, the sensitization rate in children aged one year in the high-risk Cincinnati Childhood Air Pollution Study (CCAAPS) was 28% compared to just 8% reported in children aged 1.5 years in unselected birth cohorts[1]. Epidemiologic studies consistently show an association between atopy and asthma. Atopic dermatitis (AD) is an established risk factor for asthma development and it has been estimated that one-third to half of patients with AD will develop asthma[2]. However, the sensitization rates and profiles in a cohort of children with AD are not established. We sought to compare the sensitization rates and profiles of children in CCAAPS, a high risk asthma cohort based on parental atopy, and the Mechanisms of Progression of Atopic Dermatitis to Asthma in Children (MPAACH), a high risk asthma cohort based on the presence of AD.

MPAACH is the first US-based prospective early life cohort of children with AD and the first mechanistic AD cohort designed to elucidate endotypes of AD that progress to asthma and identify biomarkers of disease progression. Inclusion criteria were: 1) aged 1–2 years upon enrollment; 2) gestation of ≥36 weeks AND 3) a diagnosis of AD (based on the Hanifin and Rajka Criteria for Atopic Dermatitis[3]), **OR** the parent(s)/legal authorized representative (LAR) indicates a positive response to each of the 3 questions from the Children's Eczema Questionnaire[4]. CCAAPS is a high-risk birth cohort of infants with at least one atopic parent, defined as symptoms of allergy and/or asthma diagnosis, and a positive skin prick test (SPT) to at least one allergen[5]. CCAAPS inclusion criteria also included a gestational age of ≥35 weeks. In CCAAPS, the definition of AD was adapted from a validated questionnaire (International Study of Asthma and Allergies in Childhood) and included a parental report of the child's scratching and redness, "raised bumps," or dry skin/scaling for at least 6 of the last 12 months[6].

Participants in both cohorts had SPTs to aero and food allergens performed as part of the study protocol. Herein we compared the SPT results at age one in both cohorts as age may affect sensitization rates. The CCAAPS cohort was skin tested to a panel of 15 aeroallergens, milk and egg as previously reported[5]. SPTs in the MPAACH cohort include 11 aeroallergens and 13 food allergens. In this analysis, we directly compare sensitization rates to dog, mold, tree, cat, grass, dust mite, ragweed, egg and milk, which were performed using the same method in both cohorts. Sensitization patterns in MPAACH (n=128) were compared to the overall CCAAPS cohort (n=712), the subset with AD (n=222), and those without AD (n=490). All data and sensitization results were analyzed via Chi squared/ Fishers Exact tests using SAS.

Demographic comparisons highlight the distinct recruitment techniques and populations of each high-risk cohort. MPAACH recruitment is conducted at an urban hospital and is comprised of 53% black race participants and 54% public insurance. In contrast, the CCAAPS cohort is a population-based cohort and includes 21% black participants ($p<0.01$) and 24% public insurance ($p< 0.01$).

When compared to the CCAAPS cohort, MPAACH children were significantly more likely to be sensitized to any allergen (42.2% vs 28.8%, p = 0.003), co-sensitized to both food and aero allergens (14.8% vs 4.2%, p=0.009), sensitized to food allergens only (28.1% vs 14.2%, p<0.001), and sensitized to aero allergens only (28.9% vs 18.8%, p=0.009, Figure 1A). At the individual allergen level, MPAACH children were also significantly more likely to be sensitized to dog (11.7% vs 1.4%, p<0.001), cockroach (5.5% vs 2.0%, p=0.029), and egg (26.6% vs 12.3%, p=0.001, Figure 1B), highlighting that children with AD are at much higher risk for developing atopy than children in a high-risk asthma cohort based on parental atopy.

In order to determine if AD was indeed driving the higher sensitization rates in MPAACH, we compared sensitization rates in children in CCAAPS with AD (AD+) to those without AD (AD−). As in MPAACH, the CCAAPS AD+ group had higher sensitization rates to any allergen (43.2% vs 22.2%, p<0.001), co-sensitization (9.0% vs 2.0%, p<0.001), food only (25.3% vs 9.2%, p<0.001), and aero only (27.0% vs 15.1%, p<0.001, Figure 1A) compared to the AD− group. The AD+ group had higher rates of sensitization to trees (10.4% vs 5.3%, p=0.014), cats (6.3% vs 1.9%, p<0.001), egg (22.6% vs 7.6%, p<0.001), and milk (7.7% vs 2.7%, p=0.002, Figure 1B). Dog sensitization was also higher in the AD+ group (2.7% vs 0.8%, p=0.048), however, it was significantly lower than the prevalence in MPAACH (11.7%, p = 0.001, Figure 1B).

Herein we show that the sensitization rate in the cohort of pediatric AD is almost 1.5 fold higher than the rate for a high risk asthma and allergy cohort, even though the rate of parental history of allergic disease was highly comparable. These results suggest AD further increases the risk of sensitization over heredity alone. Children from MPAACH and AD+ children from CCAAPS are almost twice as likely to be sensitized to any allergens and almost four times more likely to be co-sensitized to food and aero allergens. Both cohorts had increased sensitization rates when compared to the general population[7]. The MPAACH children and the CCAAPS children with AD had similar sensitization profiles despite stark demographic differences, supporting that AD independently contributes to increased sensitization risk. While it has been reported that children with AD may develop peanut and egg sensitizations through epidermal allergen exposure,[8, 9] our findings suggest cutaneous sensitization of aeroallergens as well. Future analyses of sensitization patterns in the MPAACH cohort will determine which phenotypes of AD are associated with early persistent, early transient, and late transient sensitization in children, and ultimately establish which AD phenotypes and sensitization profiles are most predictive of asthma and clinical allergy development in children.

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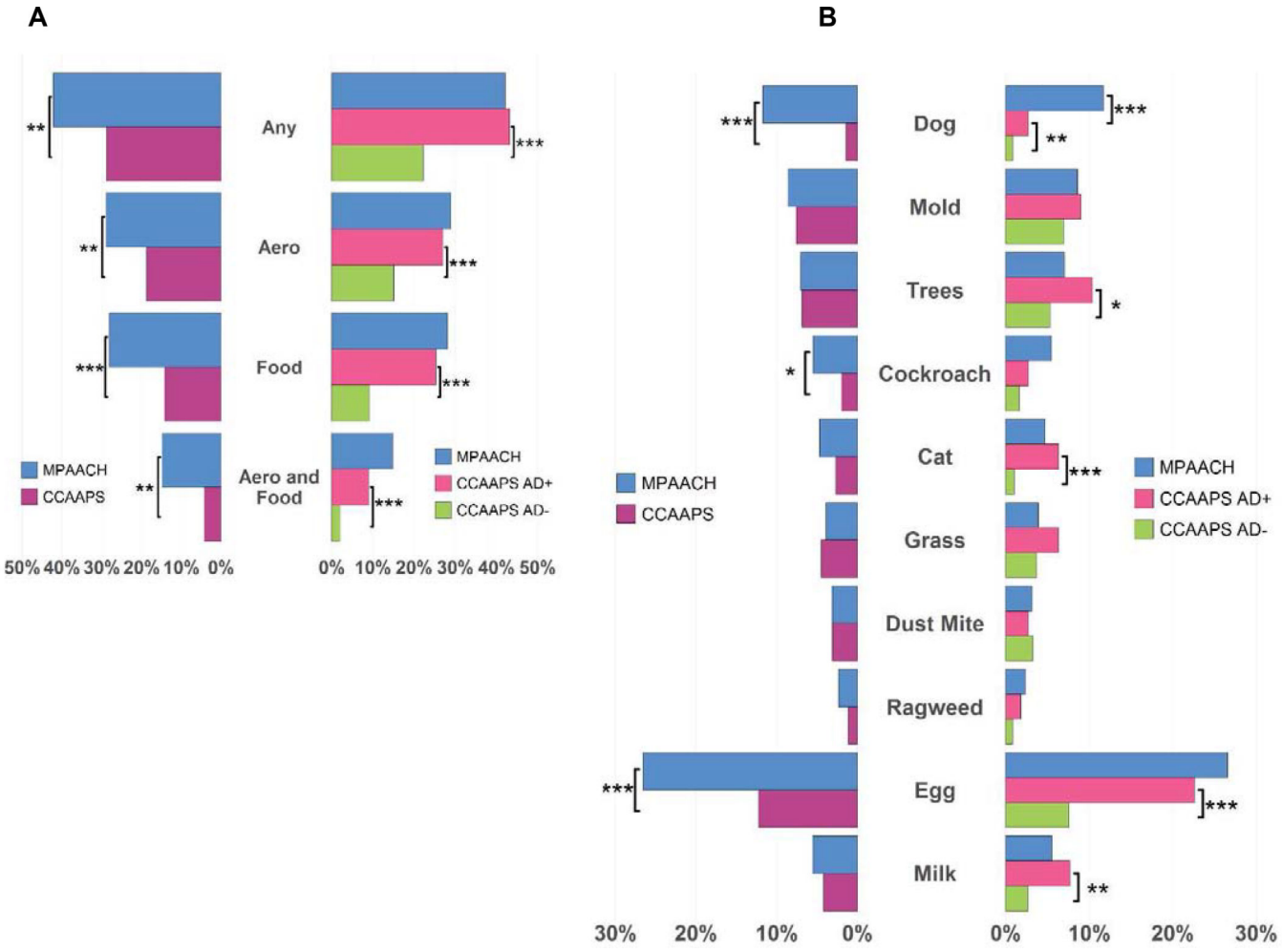

Fig 1.

Sensitization rates in the Mechanisms of Progression of Atopic Dermatitis to Asthma in Children (MPAACH) cohort and Cincinnati Childhood Air Pollution Study (CCAAPS). A) Overall rates and aeroallergen and food allergen rates in MPAACH, CCAAPS Atopic Dermatitis (AD)+ and CCAAPS AD−. B) Individual allergen sensitization rates in MPAACH, CCAAPS AD+ and CCAAPS AD−.