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Association of Atopic Dermatitis Severity With Learning Disability in Children

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IMPORTANCE Recent population-based data indicate that atopic dermatitis (AD) is associated with learning disability (LD) in children, but the association between AD severity and LD is unknown.

OBJECTIVE To evaluate the association of AD severity with learning problems in children with AD.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study analyzed data of US participants enrolled in the Pediatric Eczema Elective Registry (PEER) between November 1, 2004, and November 30, 2019. Participants were children aged 2 to 17 years at registry enrollment with physician-confirmed diagnosis of AD and had completed 10 years of follow-up in PEER.

EXPOSURES Atopic dermatitis severity measured by both the Patient-Oriented Eczema Measure (POEM) score and self-report. The POEM scores ranged from 0 to 28, with strata of clear or almost clear skin (0-2), mild (3-7), moderate (8-16), severe (17-24), and very severe (25-28). Self-reported AD severity was categorized as clear skin or no symptoms, mild, moderate, or severe.

MAIN OUTCOMES AND MEASURES Learning disability diagnosed by a health care practitioner, as reported by the participants or their caregivers.

RESULTS Among the 2074 participants with AD (1116 girls [53.8%]; median [interquartile range (IQR)] age, 16.1 [13.9-19.5] years at 10-year follow-up), 169 (8.2%) reported a diagnosis of an LD. Children with an LD vs those without an LD were more likely to have worse AD severity, as measured by the median (IQR) total POEM score (5 [1-10] vs 2 [0-6]; $P < .001$), POEM severity category (moderate AD: 50 of 168 [29.8%] vs 321 of 1891 [17.0%]; severe to very severe AD: 15 of 168 [8.9%] vs 85 of 1891 [4.5%]; $P < .001$); and self-report (moderate AD: 49 of 168 [29.2%] vs 391 of 1891 [20.7%]; severe AD: 11 of 168 [6.5%] vs 64 of 1891 [3.4%]; $P < .001$). In multivariable logistic regression models adjusted for sex, age, race/ethnicity, annual household income, age of AD onset, family history of AD, and comorbid conditions, participants with mild AD (odds ratio [OR], 1.72; 95% CI, 1.11-2.67), moderate AD (OR, 2.09; 95% CI, 1.32-3.30), and severe to very severe AD (OR, 3.10; 95% CI, 1.55-6.19) on the POEM were all significantly more likely to have reported an LD than those with clear or almost clear skin.

CONCLUSIONS AND RELEVANCE This cross-sectional study found that worse AD severity was associated with greater odds of reported LD, independent of socioeconomic characteristics, AD onset age, and other related disorders. Although additional prospective and mechanistic studies are needed to clarify the association of AD with learning, the findings suggest that children with more severe AD should be screened for learning difficulties to initiate appropriate interventions that can mitigate the consequences of an LD.

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Growing evidence indicates that atopic dermatitis (AD) in children is associated with disruptions in sleep, attention, and memory.[1-3] Recent population-based data in the US also demonstrate a greater prevalence of learning disability (LD) among children with AD compared with those without it.[4] Learning disability refers to disorders that impair areas of learning, such as reading, writing, and mathematics, and is associated with poor mental health, lower educational achievement, and worse occupational outcomes.[5]

Although children with AD appear more likely than children without AD to have an LD diagnosis, the association of AD severity with LD remains unknown. Thus, the objective of this study was to evaluate the association of AD severity with learning problems in a large cohort of US children with AD. We hypothesized that more severe AD was associated with higher rates of reported LD.

Key Points

Question What is the association of atopic dermatitis severity with learning disability in children?

Findings In this cross-sectional study of 2074 children with physician-confirmed atopic dermatitis, those with mild, moderate, or severe disease were significantly more likely to report a learning disability diagnosis by a health care practitioner compared with those with clear or almost clear skin. Worsening severity was associated with higher rates of learning disability in a dose-dependent manner.

Meaning Results of this study suggest that atopic dermatitis is associated with learning problems and that children with more severe skin disease should undergo screening and treatment for any learning difficulties.

Methods

We used data from the Pediatric Eczema Elective Registry (PEER), a prospective pediatric cohort of children with AD in the US. This registry was designed as a postmarketing study to evaluate the risk of malignant neoplasm associated with the use of pimecrolimus, a topical calcineurin inhibitor for the treatment of AD. Details of the PEER have been previously reported.[6] In brief, all participants in the PEER were aged 2 to 17 years at registry enrollment (between November 1, 2004, and November 30, 2019) and had a physician-confirmed diagnosis of AD. All participants had used pimecrolimus for at least 6 weeks in the 6-month period preceding enrollment, although they were not required to continue its use after enrollment and many did not.[7] Participants in PEER were followed up for 10 years. Written informed consent was obtained from participants at the time of registry enrollment, and the study was granted exempt status by the University of Pennsylvania Institutional Review Board because it used existing deidentified data.

In this cross-sectional study, we conducted an analysis of participants in the PEER who had completed 10 years of follow-up in the registry by November 30, 2019, given that data on LD were collected in the PEER at that time. At registry enrollment, participants or their caregivers provided information on sociodemographic characteristics, AD history and treatment, and personal and family medical history. At the 10-year follow-up, participants were asked whether they had ever been diagnosed with an LD by a health care practitioner (ie, "Has your child ever been told by your health care provider that he/she has a learning disability?"). In addition to self-reporting their AD severity in the preceding 6-month period, participants completed the Patient-Oriented Eczema Measure (POEM), a validated core outcome instrument for measuring patient-reported symptoms of AD in the past week.[8] Children with a reported diagnosis of autism were excluded from the study because clinical diagnoses of LD and autism are considered mutually exclusive, according to the *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition).[9]

The exposure of interest was AD severity. In the primary analysis, the POEM score was considered as both a continuous and a categorical variable. The POEM scores ranged from 0 to 28, with a previously established severity strata of clear or almost clear skin (0-2), mild (3-7), moderate (8-16), severe (17-24), and very severe (25-28).[10] In the secondary analysis, we evaluated self-reported AD severity, which was categorized as clear skin or no symptoms, mild, moderate, or severe. The study outcome was the diagnosis of an LD by a health care practitioner, as reported by the participant or caregiver.

Statistical Analysis

To evaluate the association between AD severity and LD, multivariable logistic regression analysis was performed to estimate the odds of an LD with respect to the POEM score or self-reported AD severity. Analyses were adjusted for potential confounders, including sex; age; race/ethnicity; annual household income; age of AD onset; family history of AD; and personal history of asthma, seasonal allergies, sleep problems, and neuropsychiatric conditions (which included attention-deficit/hyperactivity disorder [ADHD], depression, anxiety, and behavioral or conduct problems). Because ADHD is highly prevalent and can often coincide with an LD, we also conducted a sensitivity analysis that excluded participants with ADHD.

Two-tailed Mann-Whitney test was used to compare continuous variables, and 2-tailed Fisher exact test was used to compare categorical variables. Two-sided $P < .05$ indicated statistical significance. Data analysis was performed using Stata, version 14 (StataCorp LLC).

Results

A total of 2074 participants were included in the study (**Table 1**). Of these participants, 1116 were female (53.8%) and 958 were male (46.2%) children. The median (interquartile range [IQR]) age of participants was 6.0 (3.8-9.4) years at the time of initial enrollment into the PEER and was 16.1 (13.9-19.5) years at the time of their 10-year follow-up. Most participants reported Black (931 [44.9%]) or White (818 [39.4%]) race/ethnicity, and most were from households with annual incomes of $0 to $49 999 (1081 [52.1%]) or $50 000 to $99 999 (407 [19.6%]). The median (IQR) age of AD onset among participants was 0.75 (0.25-2.0) years. Asthma was reported by

1008 participants (48.6%), and seasonal allergies were reported by 1507 participants (72.7%). A family history of AD was noted in 1093 participants (52.7%) (Table 1).

At 10 years' follow-up, the median (IQR) POEM score was 2 (0-7), with 13 of 2074 participants (0.6%) having very severe AD, 88 (4.2%) having severe AD, 371 (17.9%) with moderate AD, 506 (24.4%) with mild AD, and 1083 (52.2%) with clear or almost clear skin. Self-reported AD severity over the preceding 6-month period was severe for 75 participants (3.6%), moderate for 441 (21.3%), mild for 890 (42.9%), and clear skin or none for 651 (31.4%). A total of 169 individuals (8.2%) reported an LD diagnosis. One or more of the following neuropsychiatric conditions were reported by 482 participants (23.2%): ADHD (287 [13.8%]), anxiety (228 [11.0%]), depression (156 [7.5%]), and behavioral or conduct problems (114 [5.5%]) (Table 1). Sleep problems were noted in 222 participants (10.7%).

In univariable analyses, participants with an LD were more likely to be male children, have Black or Hispanic race/ethnicity, and have lower household income compared with those without an LD (**Table 2**). In addition, asthma, ADHD, depression, anxiety, behavioral or conduct problems, and sleep problems were more common among participants with an LD than those without an LD (Table 2).

The median (IQR) total POEM score was significantly higher among children with an LD compared with those without (5 [1-10] vs 2 [0-6]; $P < .001$). Using severity categories based on the POEM score, more participants with an LD had moderate AD (50 of 168 [29.8%] vs 321 of 1891 [17.0%]) or severe to very severe AD (15 of 168 [8.9%] vs 85 of 1891 [4.5%]) in contrast to those without an LD (Table 2). Similarly, self-reported AD severity was moderate (49 of 166 [29.5%] vs 391 of 1889 [20.7%]) to severe (11 of 166 [6.6%] vs 64 of 1889 [3.4%]) in more children with an LD compared with those without an LD (Table 2).

Results of unadjusted and adjusted logistic regression analysis are shown in **Table 3**. In multivariable models, the odds of an LD increased by 5% per 1-point increase in the POEM score (odds ratio [OR], 1.05; 95% CI, 1.02-1.08) after adjustment for sex; age; race/ethnicity; household income; age of AD onset; family history of AD; and personal history of asthma, seasonal allergies, sleep problems, and comorbid neuropsychiatric disorders (Table 3). Across the POEM severity strata, children with mild AD (OR, 1.72; 95% CI, 1.11-2.67), moderate AD (OR, 2.09; 95% CI, 1.32-3.30), and severe to very severe AD (OR, 3.10; 95% CI, 1.55-6.19) were all significantly more likely to have an LD compared with children with clear or almost clear skin (**Figure** and Table 3).

In secondary analyses that used self-reported AD severity measurements, children with mild AD (OR, 1.68; 95% CI, 1.04-2.69), moderate AD (OR, 1.97; 95% CI, 1.16-3.34), and severe AD (OR, 2.48; 95% CI, 1.03-5.95) also had significantly greater odds of an LD compared with children with recently clear skin (Figure and Table 3). A sensitivity analysis that was limited to participants without reported ADHD yielded similar findings, with an OR for an LD of 1.64 (95% CI, 0.89-3.03) for mild AD, 2.42 (95% CI, 1.28-4.55) for moderate AD, and 2.78 (95% CI, 1.14-6.81) for severe to very severe AD, compared with those who reported clear or almost clear skin based on the POEM score.

Table 1. Participant Characteristics

Characteristic	No. (%) (n = 2074)
Sex	
Male	958 (46.2)
Female	1116 (53.8)
Age, median (IQR), y	16.1 (13.9-19.5)
Race/ethnicity	
White	818 (39.4)
Black	931 (44.9)
Hispanic	173 (8.3)
Asian	82 (4.0)
Other[a]	70 (3.4)
Annual household income, $	
0-49 999	1081 (52.1)
50 000-99 999	407 (19.6)
≥100 000	195 (9.4)
Prefer not to answer	389 (18.8)
Age of AD onset, median (IQR), y	0.75 (0.25-2.0)
Family history of AD	1093 (52.7)
AD severity based on the POEM score	
Total score, median (IQR)	2 (0-7)
Clear or almost clear skin: 0-2	1083 (52.2)
Mild: 3-7	506 (24.4)
Moderate: 8-16	371 (17.9)
Severe: 17-24	88 (4.2)
Very severe: 25-28	13 (0.6)
Missing	13 (0.6)
Self-reported AD severity in past 6 mo	
Clear skin or none	651 (31.4)
Mild	890 (42.9)
Moderate	441 (21.3)
Severe	75 (3.6)
Missing	17 (0.8)
Asthma	1008 (48.6)
Seasonal allergies	1507 (72.7)
Learning disability	169 (8.2)
ADHD	287 (13.8)
Sleep problems	222 (10.7)
Depression	156 (7.5)
Anxiety	228 (11.0)
Behavioral or conduct problems	114 (5.5)

Abbreviations: AD, atopic dermatitis; ADHD, attention-deficit/hyperactivity disorder; IQR, interquartile range; POEM, Patient-Oriented Eczema Measure.

[a] Included Pacific Islander, American Indian/Alaska Native, and multiracial.

Discussion

To our knowledge, this analysis is one of the first studies to examine the association between AD severity and learning problems. The findings indicated that more severe AD was associated with up to a 3-fold increase in the odds of an LD, independent of sociodemographic characteristics, AD onset age,

Table 2. Prevalence of Learning Disability by Participant and Disease Characteristics

Characteristic	Without learning disability (n = 1903), No. (%)[a]	With learning disability (n = 169), No. (%)[a]	*P* value[b]
Sex			
Male	862 (45.3)	96 (56.8)	.01
Female	1041 (54.7)	73 (43.2)	
Age, median (IQR), y	16.1 (13.9-19.5)	16.0 (13.6-19.0)	.41
Race/ethnicity			
White	767 (40.3)	51 (30.2)	<.001
Black	836 (43.9)	93 (55.0)	
Hispanic	149 (7.8)	24 (14.2)	
Asian	82 (4.3)	0 (0)	
Other[c]	69 (3.6)	1 (0.6)	
Annual household income, $			
0-49 999	966 (50.8)	113 (66.9)	<.001
50 000-99 999	381 (20.0)	26 (15.4)	
≥100 000	189 (9.9)	6 (3.6)	
Prefer not to answer	365 (19.2)	24 (14.2)	
Age of AD onset, median (IQR), y	0.75 (0.25-2.0)	0.75 (0.25-3.0)	.97
Family history of AD	993 (52.2)	99 (58.6)	.13
Asthma	910 (47.9)	98 (58.0)	.01
Seasonal allergies	1378 (72.5)	129 (77.3)	.20
Sleep problems	164 (8.6)	58 (34.5)	<.001
ADHD	194 (10.2)	93 (55.0)	<.001
Depression	115 (6.1)	41 (24.3)	<.001
Anxiety	185 (9.7)	43 (25.6)	<.001
Behavioral or conduct problems	67 (3.6)	47 (28.0)	<.001
AD severity based on POEM score			
Total score, median (IQR)	2 (0-6)	5 (1-10)	<.001
Clear or almost clear skin: 0-2	1027 (54.3)	55 (32.7)	<.001
Mild: 3-7	458 (24.2)	48 (28.6)	
Moderate: 8-16	321 (17.0)	50 (29.8)	
Severe to very severe: 17-28	85 (4.5)	15 (8.9)	
Self-reported AD severity in past 6 mo			
Clear skin or none	621 (32.9)	29 (17.5)	<.001
Mild	813 (43.0)	77 (46.4)	
Moderate	391 (20.7)	49 (29.5)	
Severe	64 (3.4)	11 (6.6)	

Abbreviations: AD, atopic dermatitis; ADHD, attention-deficit/hyperactivity disorder; IQR, interquartile range; POEM, Patient-Oriented Eczema Measure.

[a] Columns may not sum to the listed totals because of the missing data for some characteristics.

[b] Mann-Whitney test was used for continuous variables and Fisher exact test was used for categorical variables.

[c] Included Pacific Islander, American Indian/Alaska Native, and multiracial.

and other atopic and neuropsychiatric disorders. In addition, the dose-dependent association of AD severity with LD (ie, increasingly greater odds of an LD with worsening AD severity) that we observed may suggest a potential causal association in the reported association between AD and LD in a recent population-based study of US children;[4] however, causality cannot be inferred from the findings of the present study.

Existing data on the specific association between AD and learning are relatively limited to date. However, a few previous studies have examined related outcomes, such as the educational and cognitive impact of AD. Two studies found no statistically significant association between AD and educational attainment or between AD and school performance or standardized test scores after adjustment for socioeconomic factors and parental educational achievements.[11,12] One of these studies also found no association between AD and cognitive function,[11] but 2 other clinic-based studies reported lower IQ in children with AD and more symptoms of cognitive dysfunction in adults with AD.[3,13] Further research is thus needed to clarify the association of AD with learning and the mechanisms through which this association may be mediated. It is possible that symptoms of AD, such as itch and sleep impairment, may make learning more difficult.[1,14-16] Neuroinflammatory signaling in the central nervous system is also implicated in normal memory and learning,[17] and one could speculate that shared inflammatory or other pathophysiological pathways may link AD and LD. In addition, more severe AD has been associated with environmental factors, such as lower socioeconomic status, increased family stressors, and disadvantaged neighborhoods, which may increase vulnerability to cognitive or learning dysfunction.[18-22] Furthermore, other disorders such as ADHD, anxiety, and depression, which can coincide with learning dif-

Table 3. Logistic Regression Analysis of Learning Disability by Atopic Dermatitis Severity

Covariate	Unadjusted OR (95% CI)	Adjusted models, OR (95% CI)		
		Total POEM score	POEM strata	Self-reported strata
AD severity				
Total POEM score, per point[a]	1.06 (1.03-1.08)	1.05 (1.02-1.08)	NA	NA
POEM severity strata				
Clear or almost clear skin	1 [Reference]	NA	1 [Reference]	NA
Mild	1.87 (1.30-2.69)	NA	1.72 (1.11-2.67)	NA
Moderate	2.59 (1.79-3.75)	NA	2.09 (1.32-3.30)	NA
Severe to very severe	2.98 (1.68-5.29)	NA	3.10 (1.55-6.19)	NA
Self-reported severity in past 6 mo				
Clear skin or none	1 [Reference]	NA	NA	1 [Reference]
Mild	1.84 (1.25-2.73)	NA	NA	1.68 (1.04-2.69)
Moderate	2.33 (1.52-3.58)	NA	NA	1.97 (1.16-3.34)
Severe	3.09 (1.54-6.22)	NA	NA	2.48 (1.03-5.95)
Sex				
Male	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Female	0.60 (0.44-0.80)	0.62 (0.43-0.89)	0.62 (0.43-0.89)	0.65 (0.45-0.93)
Age, per y	0.98 (0.94-1.02)	0.96 (0.91-1.02)	0.96 (0.91-1.02)	0.96 (0.91-1.02)
Race/ethnicity				
White	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Black	1.63 (1.17-2.26)	1.62 (1.05-2.49)	1.58 (1.02-2.44)	1.51 (0.98-2.33)
Hispanic	2.34 (1.45-3.78)	2.38 (1.33-4.24)	2.32 (1.30-4.16)	2.26 (1.26-4.04)
Other[b]	0.42 (0.17-1.06)	0.13 (0.02-0.96)	0.12 (0.02-0.91)	0.13 (0.02-0.97)
Annual household income, $				
0-49 999	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
50 000-99 999	0.55 (0.37-0.84)	0.73 (0.43-1.23)	0.75 (0.45-1.27)	0.71 (0.42-1.19)
≥100 000	0.26 (0.12-0.57)	0.47 (0.19-1.17)	0.48 (0.20-1.20)	0.45 (0.18-1.11)
Prefer not to answer	0.58 (0.38-0.88)	0.73 (0.44-1.19)	0.74 (0.45-1.21)	0.73 (0.45-1.21)
Age of AD onset, per y	1.01 (0.96-1.06)	1.05 (0.98-1.13)	1.05 (0.98-1.13)	1.04 (0.96-1.11)
Family history of AD	1.24 (0.93-1.67)	1.11 (0.78-1.58)	1.10 (0.77-1.57)	1.12 (0.78-1.59)
Asthma	1.51 (1.12-2.02)	1.17 (0.80-1.71)	1.16 (0.79-1.70)	1.16 (0.79-1.69)
Seasonal allergies	1.39 (0.98-1.98)	0.97 (0.62-1.51)	0.98 (0.63-1.53)	0.98 (0.63-1.52)
Sleep problems	5.77 (4.16-8.02)	1.96 (1.29-2.98)	1.96 (1.29-2.98)	2.08 (1.37-3.16)
Neuropsychiatric disorders[c]	9.41 (6.83-12.96)	6.61 (4.52-9.67)	6.54 (4.46-9.57)	6.42 (4.38-9.41)

Abbreviations: AD, atopic dermatitis; NA, not applicable; OR, odds ratio; POEM, Patient-Oriented Eczema Measure.

[a] POEM severity measured as continuous variable in points.

[b] Included Asian, Pacific Islander, American Indian/Alaska Native, and multiracial.

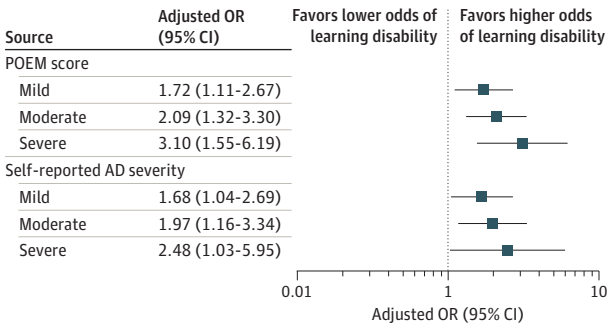
[c] Included attention-deficit/hyperactivity disorder, depression, anxiety, and behavioral or conduct problems.

ficulties and have been reported to be more common in individuals with AD,[23-25] may partially explain some of the LD observed in individuals with AD.

In this study, we adjusted for ADHD, depression, anxiety, and behavioral or conduct disorders as a composite variable that reflected comorbid neuropsychiatric disease, rather than as individual variables because (1) these conditions often overlap, (2) the data on these conditions were provided by self-report, and (3) we were primarily interested in accounting for the contribution of any neuropsychiatric comorbidity instead of obtaining specific effect estimates for each individual condition. Nevertheless, the multivariable models used to analyze ADHD as a distinct variable from the composite variable comprising depression, anxiety, and conduct problems did not meaningfully alter the findings, nor did the multivariable analyses in which ADHD, depression, anxiety, and conduct problems were included as individual covariates. Regardless of these different approaches, however, ADHD, mood disorders, and conduct problems, as well as sleep problems, may actually be factors on the causal pathway and thus may be mediators rather than confounders of the association between AD severity and LD. This possibility should be addressed in future studies, using analytic approaches such as mediation analysis or structural equation modeling, but application of these techniques in the current study was limited by the uncertain temporality and directionality among LD and other neuropsychiatric or developmental disorders in the data. In addition, the primary objective of this study was to evaluate the overall association between AD severity and LD rather than to distinguish between direct and indirect outcomes mediated by other conditions.

Because AD affects up to 20% of US children, with approximately one-third having moderate to severe disease,[18] the impact and scope of the findings of the present study may be substantial on a population level. Given that an LD has potentially lifelong implications for health, educational, and social outcomes, earlier identification (screening) and treatment of at-risk children, particularly those with moderate or

Figure. Adjusted Odds Ratios (ORs) of Learning Disability by Severity of Atopic Dermatitis (AD)



The ORs were adjusted for sex; age; race/ethnicity; annual household income; age of AD onset; family history of AD; and comorbid asthma, seasonal allergies, sleep problems, and neuropsychiatric disorders. The reference group was clear or almost clear skin for both the Patient-Oriented Eczema Measure (POEM) score and self-reported severity. Error bars represent 95% CIs.

severe AD, are thus critical for reducing the detrimental consequences of AD for learning, developing appropriate interventions, and ensuring optimal socioeducational outcomes in this patient population.

Limitations

This study has several limitations. First, the cross-sectional design of the study precluded our ability to comment on the temporal association between AD diagnosis or severity and LD. However, most participants in the PEER were diagnosed with AD before 2 years of age, and LD is generally not diagnosed in children until preschool age or more typically school age, thus making it more likely that AD onset preceded LD diagnosis in this cohort. Reverse causation, whereby the presence of an LD may have led to more severe AD at year 10 of follow-up, could not be completely excluded; however, we observed similar associations between baseline AD severity at registry enrollment and LD.

Second, outcome misclassification was a potential source of bias in this study, given that LD was measured by the participant or caregiver report of a diagnosis made by a health care practitioner. Because LD was not strictly defined in the study survey and the participants who reported a given diagnosis of an LD may not truly meet the criteria for a learning disorder, future studies should incorporate formal and direct clinical assessments of an LD. Nevertheless, a self-reported diagnosis of an LD in this study can still be taken to reflect a learning problem as perceived by a health care practitioner. An ADHD diagnosis also may be interpreted as an LD by some participants; however, the sensitivity analysis that was limited to participants without ADHD showed similar associations between AD severity and LD. Although exposure misclassification of AD severity was also possible, it was less likely because a validated severity instrument, such as the POEM, was used. Furthermore, self-reported AD severity correlated with the POEM severity.[26]

Third, given the limitations of the data in the PEER registry, we could not examine physicians' assessments of AD severity or account for other factors associated with LD, such as parental educational achievement; these will be key areas for future scientific inquiry.

Fourth, the generalizability of the findings to all children with AD may be limited by the fact that participants in the PEER were required to have previously used pimecrolimus. However, pimecrolimus is a commonly prescribed treatment for mild to moderate AD. These limitations notwithstanding, the PEER nevertheless represents a large and racially, socioeconomically, and geographically diverse population of children with physician-confirmed diagnosis of AD in the US; to our knowledge, this cohort is one of the largest pediatric AD cohorts with available data on LD.

Conclusions

Findings of this study suggest a dose-dependent association between more severe AD and learning problems. Children with more severe AD should be screened for learning difficulties so that appropriate interventions can be undertaken to mitigate the consequences of an LD. Future prospective and mechanistic studies that use direct assessments are needed to ascertain the timing and phenotypes of LD in children with AD and to clarify the direct association of AD with LD and its potential causal mechanisms.

ARTICLE INFORMATION

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Author Contributions: Dr Wan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Wan, Margolis.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Wan.
Critical revision of the manuscript for important intellectual content: All authors.
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