Atopic dermatitis is associated with multiple behavioral problems in United States children

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Abstract

Atopic dermatitis (AD) is a chronic, inflammatory skin disease associated with intense itch, sleep disturbance, psychosocial distress, and symptoms of anxiety and depression.[1] All of these sequelae of AD may negatively impact the emotional health and social functioning in children, and ultimately lead to behavioral problems. We aimed to understand the association between AD and aberrant childhood behaviors. Data were analyzed from the Fragile Families and Child Wellbeing Study, a longitudinal birth cohort study of 4898 children in 20 US cities. AD was associated with the ≥75th percentile of mean behavioral scores at 5 years (multivariable logistic regression; adjusted odds ratio [95% confidence interval]: 1.51 [1.18-1.93]), 9 years (1.62 [1.32-1.99]) and 15 years (1.44 [1.17-1.76]). There was significantly increased behavioral problems at age 15 when AD persisted at ages 5, 9 and 15 (Poisson regression; adjusted risk ratio [CI95]: 1.17 [1.01-1.35]), ages 5 and 15 (1.33 [1.08-1.63]) and ages 9 and 15 (crude risk ratio [CI95]: 1.27 [1.03-1.56]). AD was associated with 12 aberrant behaviors, particularly fighting (repeated measures logistic regression; adjusted odds ratio [CI95]: 1.40 [1.15-1.70]), physically attacking people (1.38 [1.09-1.76]), being sullen (1.31 [1.15-1.49]), worrying (1.41 [1.23-1.61]), and threatening others (1.35 [1.08-1.70]). AD at age 15 was associated with ≥75th percentile of the CBCL subscales: anxious/depressed (aOR [CI95]: 1.44 [1.16-1.78]), withdrawn (1.40 [1.11-1.77]), attention problems (1.33 [1.09-1.63]), social problems (1.39 [1.13-1.72]) and aggressive (1.49 [1.22-1.82]). Significant two-way interactions were present between AD and sleep as predictors of underactivity (4.31 [3.06-6.08]), being threatening (aOR [CI95]: 3.42 [2.20-5.34]), being sullen (3.86 [2.74-5.43]) and nervousness (4.56 [3.29-6.32]). In conclusion, childhood AD, particularly persistent disease with sleep disturbances, was associated with a wide range of behavioral problems in US children and/or adolescents.

Methods

The Fragile Families and Child Wellbeing Study (FFCWS) consists of a cohort of 4898 children, born between 1998 and 2000 in 20 urban U.S. cities.[2] FFCWS is a longitudinal study comprised of baseline in-person interviews at a child's birth (between 1998 and 2000) and follow-up telephone and/or household interviews with mothers, fathers, and/or primary caregivers at ages 1, 3, 5, 9, and 15 years.[2] The survey collects data on family characteristics, demographics, environment, health, and health behaviors. Sample weights were provided by FFCWS that adjust for the sample design, non-response at baseline, and attrition based on observed characteristics over time. Survey results yield estimates that are representative of US urban children. FFCWS was conducted as a cooperative effort by Princeton University's Center for Research on Child Wellbeing and Center for Health and Wellbeing, the Columbia Population Research Center, and the National Center for Children and Families.

- History of AD in the past year was determined by a positive response in the parent questionnaire to "In the past 12 months, has (child) had eczema or skin allergy?" that was assessed at the 5-, 9-, and 15-year follow-up interviews.
- History of sleep disturbance was determined by a positive response to "Would you say this is not true, so far as you know, sometimes true, or often true for (youth): has trouble sleeping?" that was assessed at the 5-, 9- and 15-year follow-up interview.
- The following CBCL subscales were present at each wave and selected for analysis: aggressive, withdrawn, anxious/depressed, attention problems, social problems

Statistical analysis was performed using SAS 9.4 (SAS Institute, Cary, NC). Children with data on 1-year history of AD at any of the three waves were included. Associations of 1-year prevalence of AD at each wave (5, 9 and 15 years) with sex (male/female), race (white/black/Hispanic/multiracial or other), asthma and hay fever were assessed.

Results

Table 1. Associations between AD and mean behavioral problem scores at the top 25th percentile compared to the bottom 75th percentile at 5, 9 and 15 years.

Wave	AD in past year	<75th percentile	≥75th percentile	Crude OR (95% CI)	aOR (95% CI)	Crude RR (95% CI)	aRR (95% CI)
			Percentile of behavioral problems				
5 Years	No	1871 (78.4%)	515 (21.6%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
	Yes	334 (70.9%)	137 (29.1%)	**1.49 (1.19-1.86)**	**1.51 (1.18-1.93)**	**1.13 (1.06-1.20)**	**1.13 (1.06-1.21)**
9 Years	No	1954 (75.9%)	620 (24.1%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
	Yes	362 (66.9%)	179 (33.1%)	**1.56 (1.28-1.90)**	**1.62 (1.32-1.99)**	**1.21 (1.12-1.30)**	**1.22 (1.12-1.32)**
15 Years	No	2287 (77.8%)	654 (22.2%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
	Yes	394 (70.2%)	167 (29.8%)	**1.48 (1.21-1.81)**	**1.44 (1.17-1.76)**	**1.19 (1.10-1.28)**	**1.18 (1.09-1.27)**
All	No	1217 (76.4%)	377 (23.6%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
	Yes	482 (69.6%)	211 (30.4%)	**1.41 (1.16-1.72)**	**1.29 (1.04-1.61)**	**1.15 (1.09-1.20)**	**1.13 (1.06-1.20)**

Multivariable logistic regression models were constructed with rankings of mean behavioral scores as the binary dependent variable (children were ranked either in the top 25th percentile or the bottom 75th percentile of mean behavioral scores). 1-year history of AD was the independent variable at 5-, 9- and 15-years and 1-year history AD at any of the three waves was the independent variable in the "ALL" category. Covariables included sex, age, and race/ethnicity.
Poisson regression models were constructed with the count of behavioral problems as the dependent variable (up to 24 behavioral problems in each wave) and 1-year AD history was the independent variable. Covariables included sex, age and race/ethnicity. Risk Ratios (RR) were estimated.

AD, atopic dermatitis; aOR; adjusted odds ratio; CI, confidence interval; OR, odds ratio; aRR, adjusted risk ratio; RR; risk ratio.
Bolded values indicate statistical significance. Benjamini and Hochberg corrected P-values were utilized.

Table 2. Effect AD persistence throughout childhood on behavioral problems at age 15.

AD persistence	Behavioral problems		Crude OR (95% CI)	aOR (95% CI)	Crude RR (95% CI)	aRR (95% CI)
	No	Yes				
None	1227 (77.0%)	367 (23.0%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
One wave	265 (72.6%)	100 (27.4%)	1.26 (0.98-1.63)	1.23 (0.95-1.59)	**1.18 (1.07-1.29)**	**1.17 (1.06-1.28)**
Two waves	133 (64.6%)	73 (35.4%)	**1.84 (1.35-2.50)**	**1.72 (1.26-2.34)**	**1.27 (1.13-1.42)**	**1.24 (1.10-1.39)**
5 years (early onset, transient)	87 (73.7%)	31 (26.3%)	1.19 (0.78-1.82)	1.16 (0.75-1.77)	**1.17 (1.01-1.34)**	1.15 (1.00-1.33)
9 years (intermed. onset, transient)	84 (72.4%)	32 (27.6%)	1.27 (0.83-1.95)	1.22 (0.80-1.87)	1.16 (1.00-1.36)	1.14 (0.98-1.34)
15 years (late onset)	94 (71.8%)	37 (28.2%)	1.32 (0.88-1.96)	1.31 (0.88-1.95)	**1.20 (1.04-1.39)**	**1.20 (1.04-1.38)**
5,9 years (early onset, resolving)	64 (69.6%)	28 (30.4%)	1.46 (0.92-2.32)	1.36 (0.85-2.16)	**1.23 (1.05-1.44)**	**1.20 (1.02-1.40)**
5,15 years (early onset, intermittent)	25 (59.5%)	17 (40.5%)	**2.27 (1.21-4.26)**	**2.16 (1.15-4.06)**	**1.35 (1.10-1.67)**	**1.33 (1.08-1.63)**
9,15 years (intermed. onset, persistent)	44 (61.1%)	28 (38.9%)	**2.13 (1.31-3.47)**	**1.98 (1.21-3.24)**	**1.27 (1.03-1.56)**	1.23 (1.01-1.51)
5, 9,15 years (early onset, persistent)	83 (68.0%)	39 (32.0%)	**1.57 (1.06-2.34)**	1.50 (1.00-2.24)	**1.18 (1.03-1.36)**	**1.17 (1.01-1.35)**

Multivariable logistic regression models were constructed with behavioral problems at age 15 as the binary dependent variable (children ranked in the ≥75th percentile of behavioral problems). The level of AD persistence throughout childhood was the independent variable. AD at only one of the 3 waves was classified as "one wave", and AD presence at 2 of the waves was classified as "two waves". Odds ratios (OR) and 95% CI were estimated. Multivariable Poisson regression models were constructed to estimate risk ratios (RR) and 95% CI. Covariables included sex and race/ethnicity.

AD, atopic dermatitis; aOR; adjusted odds ratio; CI, confidence interval; OR, odds ratio; aRR, adjusted risk ratio; RR, risk ratio.
Bolded values indicate statistical significance. Benjamini and Hochberg corrected P-values were utilized.

Table 3. Associations between childhood AD and individual behavioral problems.

Behavior	No AD (n=5718)	AD (n=1143)	Behavioral problem		
			Crude OR (95% CI)	aOR (95% CI)	P
Fights					
No	5176 (83.9%)	992 (16.1%)	1.00 (ref)	1.00 (ref)	
Yes	542 (78.2%)	151 (21.8%)	**1.45 (1.20-1.76)**	**1.40 (1.15-1.70)**	**0.0018**
Physically attacks					
No	5363 (83.7%)	1047(16.3%)	1.00 (ref)	1.00 (ref)	
Yes	355 (78.7%)	96 (21.3%)	**1.39 (1.09-1.75)**	**1.38 (1.09-1.76)**	**0.0126**
Sullen					
No	3481 (84.9%)	619 (15.1%)	1.00 (ref)	1.00 (ref)	
Yes	2237 (81.0%)	524 (19.0%)	**1.32 (1.16-1.50)**	**1.31 (1.15-1.49)**	**0.0003**
Worries					
No	3698 (84.5%)	680 (15.5%)	1.00 (ref)	1.00 (ref)	
Yes	2020 (81.4%)	463 (18.6%)	**1.25 (1.09-1.42)**	**1.41 (1.23-1.61)**	**0.0003**
Threatens					
No	5329 (83.7%)	1037(16.3%)	1.00 (ref)	1.00 (ref)	
Yes	389 (78.6%)	106 (21.4%)	**1.40 (1.12-1.75)**	**1.35 (1.08-1.70)**	**0.0146**

Multivariable repeated measures logistic regression models were constructed with childhood behavioral problems as the binary dependent variable and AD history as the independent variable. Covariables included sex and race/ethnicity. Responses from all 3 timepoints (5, 9 and 15 years were included). Odds ratios (OR), Adjusted Odds Ratios (aOR) and confidence intervals (CI) were estimated.
AD, atopic dermatitis; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval.
Bolded values indicate statistical significance. Benjamini and Hochberg corrected P-values are presented.

Table 4. Associations between AD and CBCL behavioral problem subscale scores at 5, 9 and 15 years.

ALL years included Subscale	AD in past year	Subscale mean score percentile <75th	≥75th	aOR (95% CI)	aRR (95% CI)
Anxious/Depressed	No	3989 (76.6%)	1215 (23.4%)	1.00 (ref)	1.00 (ref)
	Yes	742 (70.2%)	315 (29.8%)	**1.48 (1.28-1.72)**	**1.22 (1.14-1.30)**
Withdrawn	No	4298 (82.6%)	906 (17.4%)	1.00 (ref)	1.00 (ref)
	Yes	832 (78.7%)	225 (21.3%)	**1.31 (1.11-1.55)**	**1.16 (1.08-1.25)**
Attention	No	3877 (74.5%)	1327 (25.5%)	1.00 (ref)	1.00 (ref)
	Yes	758 (71.7%)	299 (28.3%)	**1.22 (1.05-1.42)**	**1.11 (1.04-1.19)**
Social	No	4120 (79.2%)	1084 (20.8%)	1.00 (ref)	1.00 (ref)
	Yes	794 (75.1%)	263 (24.9%)	**1.27 (1.09-1.49)**	**1.11 (1.04-1.19)**
Aggressive	No	3938 (75.7%)	1266 (24.3%)	1.00 (ref)	1.00 (ref)
	Yes	721 (68.2%)	336 (31.8%)	**1.45 (1.25-1.68)**	**1.10 (1.05-1.16)**

Multivariable repeated measures logistic regression models were constructed with childhood behavioral problems as the binary dependent variable and AD history as the independent variable. Responses from subscales at all 3 waves (5, 9 and 15 years) were included. Covariables included sex, age and race/ethnicity. Adjusted Odds Ratios (aOR) and confidence intervals (CI) were estimated.

Poisson regression models were constructed with number of behavioral problems in each subscale as the binary dependent variable and 1-year AD history was the independent variable. Covariables included sex and race/ethnicity. Adjusted Risk Ratio (aRR) and confidence intervals (CI) was estimated.

AD, atopic dermatitis; aOR; adjusted odds ratio; CI, confidence interval; aRR, adjusted risk ratio.
Bolded values indicate statistical significance. Benjamini and Hochberg corrected P-values were utilized.

Table 5. Associations between childhood AD with sleep and behavioral problems.

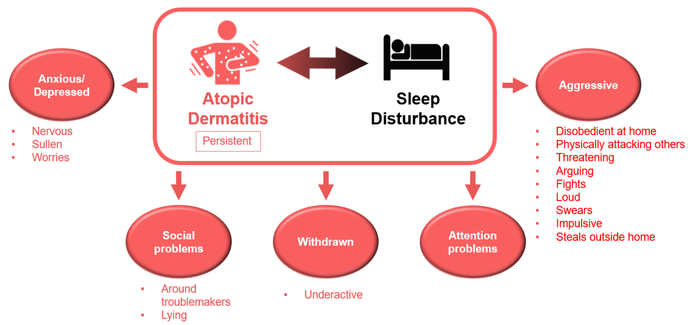
AD	Sleep				
		Underactive			
		No	Yes	aOR (95% CI)	P
No	No	4343 (89.3%)	522 (10.7%)	1.00 (ref)	
No	Yes	419 (68.5%)	193 (31.5%)	**3.87 (3.18-4.70)**	**0.0003**
Yes	No	836 (88.7%)	107 (11.3%)	1.06 (0.85-1.32)	0.6628
Yes	Yes	104 (65.8%)	54 (34.2%)	**4.31 (3.06- 6.08)**	**0.0003**
AD	**Sleep**		**Sullen**		
		No	Yes	aOR (95% CI)	P
No	No	3156 (64.9%)	1709 (35.1%)	1.00 (ref)	
No	Yes	232 (37.9%)	380 (62.1%)	**3.11 (2.60-3.70)**	**0.0003**
Yes	No	557 (59.1%)	386 (40.9%)	**1.25 (1.09-1.45)**	**0.0042**
Yes	Yes	51 (32.3%)	107 (67.7%)	**3.86 (2.74-5.43)**	**0.0003**
AD	**Sleep**		**Nervous**		
		No	Yes	aOR (95% CI)	P
No	No	4159 (85.5%)	706 (14.5%)	1.00 (ref)	
No	Yes	385 (62.9%)	227 (37.1%)	**3.35 (2.79-4.03)**	**0.0003**
Yes	No	779 (82.6%)	164 (17.4%)	**1.30 (1.08-1.57)**	**0.0100**
Yes	Yes	90 (57.0%)	68 (43.0%)	**4.56 (3.29-6.32)**	**0.0003**
AD	**Sleep**		**Lies**		
		No	Yes	aOR (95% CI)	P
No	No	3570 (73.4%)	1295 (26.6%)	1.00 (ref)	
No	Yes	351 (57.4%)	261 (42.6%)	**2.17 (1.82-2.59)**	**0.0003**
Yes	No	647 (68.6%)	296 (31.4%)	**1.22 (1.05-1.43)**	**0.0153**
Yes	Yes	84 (53.2%)	74 (46.8%)	**2.50 (1.81-3.45)**	**0.0003**

Multivariable repeated measures logistic regression models were constructed with childhood behavioral problems as the binary dependent variable. AD history and sleep were the independent variables and a two-way term between AD and asthma was constructed. Covariables included sex and race/ethnicity. Significant two-way interactions between eczema and sleep were present. Responses from all 3 timepoints (5, 9 and 15 years were included). Adjusted Odds Ratios (aOR) and confidence intervals (CI) were estimated.

AD, atopic dermatitis; aOR; adjusted odds ratio; CI, confidence interval.
Bolded values indicate statistical significance. Benjamini and Hochberg corrected P-values are presented

Conclusions

- This study demonstrated associations between AD and behavioral problems at ages 5, 9 and/or 15 years overall, particularly disobedience at home, fighting, physically attacking people, impulsiveness, hanging around troublemakers, loudness, arguing, worrying, lying and threatening.
- AD in children aged 5 years who did not have behavioral problems was associated with behavioral problems at age 9 and 15 years. These results suggest that AD preceded the onset of behavioral problems. Further, more persistent AD throughout childhood was particularly associated with behavioral problems at age 15 years.
- There were associations present between AD and the following CBCL subscales: anxious/depressed, withdrawn, attention, social and aggressive.
- Finally, there were significant interactions between AD and sleep as predictors of many behavioral problems, especially worrying, underactivity, being sullen and nervousness.



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