

Neurocognitive functioning in children with mild and moderate asthma in the Childhood Asthma Management Program

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Background: The Childhood Asthma Management Program (CAMP) is a multicenter double-blind, randomized, placebo-controlled, clinical trial of two anti-inflammatory agents and placebo in children with mild and moderate asthma.

Objective: The interrelationship between asthma severity and neurocognitive functioning among 1041 children (age range, 5-12 years) enrolled in the CAMP trial was examined.

Methods: Asthma severity was established at baseline with a clinical history of asthma symptomatology and measures of lung function (spirometry and methacholine challenge). Diary cards were used in a screening to record nighttime awakenings and doctor contacts caused by asthma symptoms, symptom severity, and number of puffs from a rescue inhaler. All children received a comprehensive neurocognitive assessment at the end of the 28-day screening period (before randomization), including measures of intelligence, attention, memory, and academic achievement.

Results: Significant differences were found between children with mild and moderate asthma on lung function and symptom outcome variables ($\log_e$ FEV₁/PC₂₀, Δ FEV₁ percent predicted, change in peak flow percent predicted, nighttime awakenings caused by asthma, average symptom severity score, and average daily number of puffs from a rescue inhaler) but not on neurocognitive variables. Multiple regression analyses revealed that asthma outcomes could not be predicted by neurocognitive variables despite controlling for socioeconomic status. The prevalence of neurocognitive dysfunction, as indicated by the use of psychostimulant medication, was found to be consistent with that found in the existing literature.

Conclusion: Mild and moderate asthma symptoms are not related to neurocognitive functioning in the children enrolled in CAMP. Mean performance on neurocognitive variables was found to be similar to that of national normative data. (*J Allergy Clin Immunol* 2000;105:717-24.)

Key words: Childhood Asthma Management Program, asthma severity, neurocognitive functioning

A variety of neurodevelopmental findings have been described in children with asthma, including an increased risk of poor school performance,¹ deficient neurocognitive performance,^{2,3} attention deficits,⁴ and developmental psychopathologies.⁵ Research interests have focused on asthma and neurocognitive outcomes,^{6,7} as well as on medication effects on neurocognitive functioning.⁸⁻¹⁰ Of particular concern are the potential effects of inhaled steroids on children's growth.¹¹⁻¹³ Less certain are the effects of inhaled steroids on children's brain development, although there is reason to suspect an indirect effect of exogenous steroids on a developing nervous system.¹⁴ Methodological shortcomings, such as sampling bias and small sample sizes,¹⁵ have raised doubts about the generalizability of previous findings. Additionally, studies that have included only children with severe asthma have greatly restricted the generalizability of findings to children with mild-to-moderate asthma.

The present report examines the relationship between illness severity variables (including interview data, diary card ratings, and lung function data) and neurocognitive functioning of children with mild-to-moderate asthma before their randomization into a clinical trial. The participants in this ongoing, multicenter, double-blind, randomized, placebo-controlled trial of over 1000 five- to twelve-year-old children with mild-to-moderate asthma were studied to test the hypothesis that neurodevelopmental impairment will be increased in children with asthma and will correlate with indices of disease severity.

METHODS

Subjects

Subjects included children ($n = 1041$) and families who were enrolled in the Childhood Asthma Management Program (CAMP) trial at 8 clinical centers. Demographic characteristics of the population are presented in Table I. The children's mean age was 8.90 years (SD, 2.12), and 32% of the study participants were from minority population groups. All neurocognitive and lung function measurement data used herein were collected in the baseline screening period when the only medication the children received was inhaled bronchodilator as needed for symptoms or prednisone for exacerbations.

Measures

Interview data. During the first prerandomization clinic visit, a structured interview with the parents was conducted by a nurse or

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*See Appendix for complete CAMP Credit Roster.

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Abbreviations used

CAMP: Childhood Asthma Management Program
 IQ: Intelligence quotient
 SES: Socioeconomic status

TABLE I. Sample characteristics (n = 1041)

Variable	n	%
Sex (female)	420	40.3
Income*		
<\$15,000	67	6.5
\$15,000-\$29,999	175	16.9
\$30,000-\$49,999	334	32.2
>\$50,000	424	40.9
Decline to state	23	2.2
Unknown	13	1.3
Total	1036†	
Ethnicity		
Non-Hispanic white	711	68.3
African American	138	13.3
Hispanic	98	9.4
Asian	21	2.0
Native American	15	1.4
Other-multiracial	58	5.6
Total	1041	
Parent education level		
<High school graduate	33	3.2
High school graduate	152	14.6
Some college	439	42.2
College graduate	416	40.0
Total	1040†	
Rating of asthma severity		
Mild	498	48.0
Moderate	543	52.0
Total	1041	
Age‡	8.9 ± 2.1	
Age of asthma onset‡		
Mild	3.3 ± 2.6	
Moderate	2.8 ± 2.3	

*Canadian dollars are considered equivalent to American dollars in this analysis.

†Total less than 1041 because of missing data.

‡Mean ± SD.

TABLE II. Factor analysis of lung function and asthma symptom data

	Factor 1	Factor 2
Lung function variables		
log _e FEV ₁ PC ₂₀	-0.200	-0.514
Change in FEV ₁ % predicted	0.027	0.818
Change in peak flow % predicted	-0.212	0.783
Symptom variables		
Nights awake	0.596	-0.027
Doctor contacts	0.414	-0.152
Average symptom severity score	0.800	0.002
No. of puffs of rescue medication	0.730	0.176
Eigenvalues	2.22	1.18
α Reliability	0.41	0.30
Variance explained	31.7%	16.8%

physician to obtain the child's asthma history. Interviewers were trained and certified in CAMP procedures.¹⁶ Data obtained from this interview and used in the following data analyses included school days missed in the past year because of asthma, hospitalizations during the past year, concurrent medications being used by the child (eg, psychostimulant medications), and a rating of asthma severity based on clinical interpretation of the information in the interview history. Severity was rated as none, mild, moderate, or severe. Children whose severity was rated as none or severe were excluded from further consideration for the trial.

Asthma diary card ratings. Diary card ratings of asthma symptoms were obtained from a 28-day screening period preceding randomization into the trial, during which children could use only their rescue inhaler (albuterol) for asthma symptoms. Data selected for analysis included the following: average severity score (ie, the mean of the daily severity scores for the 28-day screening period), the number of nights awakening from asthma, average morning and evening recorded peak flows, average daily puffs of rescue medication, and number of contacts with a doctor's office because of asthma during the 28-day screening period. An asthma code rating of 0 to 3 was recorded daily by the child or parent on the basis of the symptoms experienced during the day. Ratings were as follows: 0 indicates no asthma episodes; 1 indicates 1 to 3 mild asthma episodes, each lasting 2 hours or less; 2 indicates 4 or more mild asthma episodes or 1 or more asthma episodes that temporarily interfered with activity, play, school or sleep; and 3 indicates 1 or more asthma episodes lasting longer than 2 hours or resulting in shortening normal activity, seeing a physician, or going to the hospital.

Lung function data. Airway responsiveness and lung function were measured during the baseline period with methacholine challenge and spirometry. These procedures were completed at the third and randomization clinic visits, respectively, by a pulmonary function technician specifically certified for CAMP procedures. Ten serial dilutions of methacholine were prepared for all CAMP centers by the University of Iowa School of Pharmacy. A standardized procedure for administration of methacholine by means of a Wright nebulizer was followed.¹⁷ The spirometry system used was a Survey III Dry-seal (W.E. Collins, Braintree, Mass), which was connected to a Dell computer (model 450M or 325N) for data coding and storage. The spirometry software was developed by S & M Instrument Company and is similar to that used in other large clinical trials.¹⁸ To compare children across different ages, heights, race-ethnicity, and sexes, data from spirometry testing were analyzed as a percentage of predicted value.^{19,20} Spirometry variables included prebronchodilator FEV₁ (L) and postbronchodilator FEV₁ (L). Prebronchodilator and postbronchodilator peak flow (L/min) and peak expiratory flow rate were measured on a peak flowmeter.

Wechsler Intelligence Scales (WISC-III/WPPSI-R). The Wechsler Scales^{21,22} are recent measures of general intelligence for children. With both the WISC-III and the WPPSI-R, short forms were used because data indicate that short-form triads correlate well with standard long-form scores ($r^2 = 0.878$).²³ The triad of Similarities, Vocabulary, and Block Design was administered to all children, with those below age 6 years being administered the WPPSI-R. A deviation intelligence quotient (IQ) score ($x = 100$; $SD = 15$) was generated from the subtests of Similarities, Vocabulary, and Block Design (Sattler, 1991) and used in the analyses.

Woodcock-Johnson Psychoeducational Battery—Revised. The Woodcock-Johnson Psychoeducational Battery—Revised²⁴ is one of the most frequently used measures of educational achievement. Academic achievement was assessed by administration of the 3 skills cluster subtests, which included Letter-Word Identification, Dictation, and Applied Problems. A composite standard score for the skills cluster items was used in the analyses ($x = 100$; $SD = 15$).

TABLE III. Mean scores for mild and moderate asthma groups and asthma severity and neurocognitive variables

Variable	n	P value	x Mild (SD) (n = 498)	x Moderate (SD) (n = 543)	x Total (SD)
Asthma severity variables					
Log _e FEV ₁ PC ₂₀	1038	<.0001	0.33 (1.16)	−0.03 (1.17)	0.14 (1.18)
Change FEV ₁ % predicted	1029	.0001	7.97 (6.72)	10.10 (7.73)	9.08 (7.34)
Change in peak flow % predicted	1010	NS	12.23 (14.77)	13.06 (16.61)	12.67 (15.76)
Night awakenings*	1041	.0001	0.66 (1.32)	0.99 (1.62)	0.84 (1.50)
Doctor contacts*	1041	NS	0.04 (0.23)	0.05 (0.26)	0.05 (0.25)
Average symptom severity score*	1041	.0001	0.54 (0.32)	0.65 (0.36)	0.60 (0.34)
Mean daily No. of puffs of rescue medication*	1041	<.0001	1.24 (1.23)	1.70 (1.49)	1.48 (1.39)
Neurocognitive variables					
WISC-III/WPPSI-R IQ score†	1034	NS	105.96 (14.83)	106.02 (15.74)	105.99 (15.31)
WRAML Memory Screening Index†	1034	NS	105.57 (14.23)	104.74 (13.41)	105.14 (13.81)
GDS delay-inhibition task†	1033	NS	99.96 (14.01)	99.01 (13.98)	99.47 (13.99)
GDS simple attention: correct†	1022	NS	99.04 (15.81)	97.66 (16.20)	98.32 (16.02)
GDS simple attention: commission errors†	1022	NS	90.92 (16.08)	89.75 (16.43)	90.31 (16.27)
GDS complex attention: correct (CAcor)†‡	896	NS	100.33 (16.79)	100.61 (17.02)	100.47 (16.89)
GDS complex attention: commission errors†‡	896	NS	88.70 (17.84)	88.90 (17.93)	88.80 (17.88)
WJ-R skills cluster score†	1033	NS	105.18 (13.37)	104.02 (14.12)	104.58 (13.77)

NS, Not significant; WJ-R, The Woodcock-Johnson Psychoeducational Battery—Revised.

*Nonnormally distributed data tested by using the Wilcoxon 2-sample test.

†Standard scores (X = 100; SD = 15).

‡Measure done only on children ages 6–18 years of age.

Wide Range Assessment of Memory and Learning (WRAML). The Wide Range Assessment of Memory and Learning (WRAML)²⁵ provides a broad-based assessment of children's memory. Validity has been established with other measures of children's memory, including the McCarthy Scales of Children's Abilities ($r^2 = 0.72$) and the Stanford-Binet fourth edition ($r^2 = 0.80$). Subtests comprising the memory screening index (ie, picture memory, design memory, verbal learning, and story memory) were administered to all children. The memory screening index standard score (x = 100; SD = 15) was used in the analyses.

Gordon Diagnostic Systems. The Gordon Diagnostic Systems (GDS)²⁶ is a portable self-contained device that administers 3 different types of attention tasks: a delay task, a vigilance task, and a distractibility task. The GDS measures correct responses, omissions, commission errors (total and subtype commission errors), and response latencies. Three tasks from the GDS were administered in the current study: the Delay, Vigilance, and Distractibility subtests. In the data analyses standard scores (x = 100; SD = 15) were used from the Delay task (total correct), Vigilance task (total correct and total commission errors), and the Distractibility task (total correct and total commission errors).

Psychiatric medication use. Parents were asked to list all medications being used by their child at the time of the baseline interview. Psychiatric medications were categorized as either psychostimulant, antidepressant, or other (eg, neuroleptic medication), and the numbers of children who were using each type of medication were calculated.

Procedures

All data for the current study were collected during the baseline screening period, which began with the subject's enrollment and ended with randomization to a treatment group. This study had been approved by the human subjects review committee at each of the participating institutions before beginning enrollment procedures. At enrollment, a baseline asthma history was obtained through a structured clinical interview of the parent by a coordinator or physician, and informed consent was obtained. Additional procedures are described elsewhere.¹⁶ Neurocognitive and psychosocial data were

collected at the end of the 28-day drug washout period shortly before randomization into one of the treatment arms (active medications or placebo).

All neurocognitive and psychosocial data were obtained by a psychometrist trained and certified in administration of these measures. Procedures were standardized across all CAMP clinical centers through training, certification, and use of a CAMP-specific test administration and scoring manual.²⁷ An identical order of test administration was maintained throughout the CAMP centers (WISC-III, The Woodcock-Johnson Psychoeducational Battery—Revised, WRAML, and GDS). A protocol was established for the standardized administration of measures of attention (GDS) and memory (WRAML) to ascertain a measure of long-term verbal recall and recognition memory. The WRAML memory screening index subtests were administered in the standardized manner (ie, picture memory, design memory, verbal learning, and story memory), including the administration of the delayed recall of the items from the verbal learning subtest. Immediately after the delayed recall of these items, the child was administered the 3 GDS subtests (ie, Delay, Vigilance, and Distractibility). After this procedure, the child was administered the delayed free recall portion and then the recognition memory portion of the Story Memory task. This procedure assured a standardized time interval (30 minutes), after which long-term verbal recall and recognition memory were assessed. Breaks in the testing session were provided on the basis of the judgment of the psychometrist. However, to maintain a standardized time interval for long-term recall and recognition portions of the story memory subtest, no breaks were allowed during this interval in the protocol. All neurocognitive data were obtained in a single visit. Scoring of tests was performed by the psychometrist and checked by the psychologist at each clinical center.

Data reduction and analysis

To determine the best combination of independent lung function and diary card variables for characterizing asthma severity, independent variables were selected a priori for factor analysis. Postbronchodilator minus prebronchodilator changes in FEV₁ and peak expiratory flow rate were evaluated. Methacholine responsiveness is a

TABLE IV. Correlation matrix for asthma variables and selected neurodevelopmental variables

	$\log_e \text{FEV}_1 \text{PC}_{20}$	Change in FEV_1 % predicted	Change in peak flow % predicted	Nights awake	Doctor contacts
$\log_e \text{FEV}_1 \text{PC}_{20}$	1.00				
Change FEV_1 % predicted	-0.35†	1.00			
Change in peak flow % predicted	-0.10*	0.36†	1.00		
Nights awake	-0.14†	0.18†	0.04	1.00	
Doctor contacts	-0.04	0.04	0.04	0.12†	1.00
Average symptom code	-0.17†	0.19†	0.09	0.27†	0.08
Average No. of rescue puffs	-0.27†	0.28†	0.15†	0.22†	0.14†
IQ	0.02	-0.04	-0.08	0.02	-0.03
MSI	0.04	-0.04	-0.10	-0.03	-0.00
D-I	0.03	-0.04	0.02	0.01	0.01
SAcor	-0.05	0.01	-0.07	0.04	-0.01
SAcom	-0.04	0.00	-0.08	0.04	-0.03
CAcor	-0.02	0.04	-0.09	0.05	-0.02
CAcom	-0.02	0.03	0.04	0.02	-0.01
WJ-SC	0.01	-0.02	-0.07	0.06	0.01

$\log_e \text{FEV}_1 \text{PC}_{20}$, Logarithmic transformation of methacholine responsiveness; *Nights awake*, nights awake during the 28-day screening; *Doctor contacts*, physician contacts for asthma during the 28-day screening; *Avg Sym Code*, average asthma severity score; *MSI*, Memory Screening Index; *D-I*, Delay-inhibition task (GDS Delay task); *SAcom*, simple attention: correct (GDS Vigilance: correct); *SAcor*, simple attention: commission errors (GDS Vigilance: commission errors); *CAcor*, complex attention: correct (GDS Distractability: correct); *CAcom*, complex attention: commission error (GDS Distractability: commission errors); *WJ-SC*, Skills Cluster score.

* $P < .001$.

† $P < .0001$.

continuous variable that has a highly skewed distribution. To improve the normality of the distribution of methacholine responsiveness, the data were logarithmically transformed ($\log_e \text{FEV}_1 \text{PC}_{20}$). Diary card variables selected to characterize asthma severity included nighttime awakenings from asthma symptoms, physician contacts caused by asthma, symptom severity score, and the number of puffs from rescue medication for symptoms during the 28-day screening period.

Lung function measures were assumed to be correlated with measures from diary cards and as such were examined with an oblique rotation factor analysis. The oblique rotation was selected a priori because the investigators assumed that the resulting factors would be correlated. Results (Table II) reveal two separate factors, one characterized by lung function and the other characterized by diary card symptom data. Eigenvalues and coefficient α values indicate relatively low internal consistency of the factor variables. An α reliability of less than .70 is considered inadequate because the items are not sufficiently correlated and do not warrant scoring.²⁸ A factor score with an α value below .70 would not necessarily correspond with other severity parameters. Thus no further analyses were performed with these factors. Subsequent analyses examined each measure of asthma severity as an individual variable rather than a factor score.

Additional statistical analyses included *t* tests for differences between mild and moderate asthma groups on the independent variables selected above. Where descriptive statistics indicated a skewed distribution, the Wilcoxon signed rank test was used.²⁹

RESULTS

Descriptive statistics of the variables used to examine the questions for this study are presented in Table III. The data for IQ, memory, attention, delay, and academic achievement measures appear to be normally distributed, with means and SDs similar to those reported for normative groups. That is, as a group, children in the CAMP trial score at levels that would be considered normal on

these measures. In contrast, the children in the CAMP trial scored lower than reported norms on the GDS commission error scores (simple and complex attention), each by approximately two thirds of an SD.

Comparisons between children with mild and moderate asthma were made by using the coordinator-physician asthma severity rating. Two sample *t* tests were used to compare the mild and moderate groups; however, nonparametric methods (ie, Wilcoxon 2-sample tests) were also used for measures with skewed distributions, such as the number of puffs of rescue inhaler taken for symptoms. There were significant differences between groups on major asthma outcome variables ($\log_e \text{FEV}_1 \text{PC}_{20}$), the change in FEV_1 percent predicted, nighttime awakenings from asthma symptoms, average symptom severity score, and number of puffs from rescue inhaler for symptoms. Parametric (*t* tests) and nonparametric tests yielded similar results. The between-group differences are noteworthy because the ratings of asthma severity were obtained in the structured initial baseline history interview, which occurred before the 28-day screening period. Thus the rating of asthma severity was not influenced by knowledge of lung function variables or diary card data.

Correlations were calculated between lung function, asthma severity variables, and neurocognitive functioning indicators (Table IV). There are significant correlations between symptom-related diary card information and lung function data. Lung function variables and asthma symptoms, however, did not significantly correlate with neurocognitive variables, suggesting that there is no relationship between mild and moderate asthma and neurocognitive functioning. In contrast, significant relationships were present among the neurocognitive variables,

Average symptom code	Average No. of rescue puffs	IQ	MSI	D-I	SAcor	SAcom	Cacor	CACom	WJ-SC
1.00									
0.56†	1.00								
0.05	0.01	1.00							
0.01	0.01	0.43†	1.00						
0.05	0.02	0.18†	0.08	1.00					
0.05	0.04	0.26†	0.25†	0.12†	1.00				
0.05	0.05	0.26†	0.19†	0.05	0.44†	1.00			
0.08	0.03	0.32†	0.21†	0.11*	0.48†	0.29†	1.00		
0.09	0.06	0.26†	0.15†	0.09	0.32†	0.63†	0.41†	1.00	
0.01	0.03	0.58†	0.37†	0.17†	0.33†	0.25†	0.34†	0.23†	1.00

which were apparent even when sociodemographic variables were controlled (eg, IQ and memory $r^2 = 0.43$).

An attempt to assess whether socioeconomic status (SES), race-ethnicity, and neurocognitive variables could predict asthma outcomes was undertaken by developing a general linear model with multiple regression. Outcomes (dependent variables) selected for analysis included the following: $\log_e \text{FEV}_1 \text{PC}_{20}$, the change in FEV_1 percent predicted, average asthma severity score, and average puffs of rescue medication during the 28-day screening period. The initial regression equation examined only SES and race-ethnicity variables, and the second examined neurocognitive variables after controlling for SES and race-ethnicity. These variables were entered into the regression equation simultaneously as independent variables and specifically included income level, respondent education level, and race-ethnicity. Neurocognitive variables included all variables previously identified in Table III. Results indicated that only 2% of the variance was accounted for in the equations by SES and race-ethnicity, and the addition of neurocognitive variables did not account for any additional variability. These findings indicate again that there is no relationship between these asthma severity measures and neurocognitive measures.

Neurocognitive dysfunction among our subjects was additionally examined by determining the frequency of reported treatment with psychiatric medications and in particular psychostimulant medications used in the treatment of attention deficit hyperactivity disorder. The base rate for use of psychostimulant medication is 3.2%, which is roughly equivalent to findings from large epidemiologic studies in which 2.8% of children within the same age group were found to be taking psychostimulant

medications.³⁰ Within the CAMP population, a total of 3.8% of children were reported to have ever been treated with psychiatric medications of any type, including 3.2% who were being treated with psychostimulant medication at enrollment.

DISCUSSION

In this large multicenter study no increase in neurocognitive difficulty was identified in children with mild-to-moderate asthma when compared with normative data from standardized neuropsychological tests. Furthermore, asthma severity was not correlated with any of the neurocognitive variables, and use of psychostimulant medication was not any higher than levels of use in the general pediatric population. Despite findings from previous studies indicating that children with asthma are at risk for various types of neurocognitive dysfunction,²⁻⁴ those conclusions were not confirmed by the present study. The current findings suggest that previous estimates of neurocognitive dysfunction may have been overstated.

Of particular interest was the finding that CAMP children scored between two thirds and one SD below the normative value on a measure of impulse control, the GDS commission errors for the Vigilance, and Distractibility tasks (Table III). Although there was no difference between subjects with mild and moderate asthma on these measures, the entire group mean score suggests difficulties with the modulation and control of impulsive behaviors. Whether this finding has implications for appropriate use of asthma medications, subsequent neurocognitive dysfunction, or psychosocial adjustment of these children remains to be seen. A finding of further

interest to pediatric asthma researchers was the lack of relationship between asthma severity and academic competence. In fact, CAMP children demonstrated an average level of academic performance on the Woodcock Skills Cluster score.

The attempt to develop a global rating of asthma severity through factor analysis was abandoned when analysis revealed that the variables have a poor internal reliability and hence the decision to treat asthma severity as separate variables in further analyses. Although the factors correlate with each other, they do not represent a strong model for assessing asthma severity among children with mild and moderate asthma. These findings are similar to those of other investigators who have suggested that measures of asthma severity need to be treated independently when examining the clinical course of asthma.³¹

Whereas a relationship between neurocognitive outcomes and asthma severity has been found to vary across previous studies, the current results indicate that there is no relationship between these constructs in a large culturally diverse group of children with mild and moderate asthma. Given the association of socioeconomic variables with asthma severity³²⁻³⁴ and neurocognitive functioning,^{35,36} we were surprised to find that attempts to predict asthma severity from neurocognitive data were unsuccessful, even when controlling for socioeconomic status.

The prevalence of pharmacologic treatment for neurocognitive dysfunction in this population suggests that the prevalence of neurocognitive dysfunction in children with mild and moderate asthma ranges from 2% to 3%, which is well below the estimated prevalence of neurodevelopmental dysfunction, which has been reported in children with severe asthma.⁵ In fact, the percentage of children under treatment with psychostimulant medications found in this study does not exceed that of studies of general populations of school-age children.³¹

What is the explanation for a low base rate of neurocognitive dysfunction in the CAMP population? This finding could reflect an unrecognized selection bias occurring during the baseline protocol. The rigorous baseline protocol, including children being managed on an as-needed bronchodilator for the 28-day screening period, may have skewed the study population toward the mild end of the asthma spectrum. However, the current findings identify how global ratings of mild and moderate asthma do correspond with selected diary card and lung function data. In fact, between-group differences in FEV₁ percent predicted do reveal that children with moderate asthma are more reversible than those with mild asthma, indicating distinct asthma severity groups. It is also possible that the rigorous baseline protocol excluded children with manifest neurocognitive dysfunction that could interfere with compliance. That is, the requirement of multiple clinic visits, maintaining diary cards, and other clinical demands of the study may have been too taxing for these families.

In summary, the baseline examinations of children participating in the CAMP trial show no relationship between asthma severity and neurocognitive difficulties. Results from this study can be generalized only to chil-

dren with mild-to-moderate asthma. Children with severe asthma may experience a variety of events that increase the risk for neurocognitive impairment, including frequent school absence,⁶ markedly decreased physical activity,³⁷ frequent treatment with oral corticosteroids, and in more extreme cases episodes of respiratory arrest and hypoxia.^{38,39} Consequently, it remains essential that indices of asthma severity are carefully documented in any further investigation of the relationship between childhood asthma and neurocognitive development.

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