

# Infant Malnutrition Is Associated with Persisting Attention Deficits in Middle Adulthood<sup>1–3</sup>

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## Abstract

Infantile malnutrition is known to be associated with cognitive and behavioral impairment during childhood and adolescence. Data pertaining to longer-term effects on behavioral outcomes in adulthood are limited. In this study, we report associations between infantile malnutrition and attention problems in adults at midlife. Attention problems were assessed by the Conners Adult ADHD Rating Scales (CAARS) and the Conners Continuous Performance Test (CPT) in 145 Barbadian adults (aged 37–43 y) who had been followed longitudinally since childhood. Previously malnourished participants ( $n = 80$ ) had experienced moderate to severe protein-energy malnutrition in the first year of life and were successfully rehabilitated thereafter. They were compared with healthy adults ( $n = 65$ ) who were former classmates of the index cases and who had been matched for age, sex, and handedness in childhood. Multiple regression analyses showed persisting effects of childhood malnutrition on both the CAARS and the CPT, independent of effects of household standard of living assessed in childhood. The malnutrition effect on the CAARS ratings was independent of IQ, whereas this effect was attenuated for the CPT after adjustment for IQ. Teacher-reported attention problems in childhood predicted attention problems in adulthood, indicating continuity over the life span. Infantile malnutrition may have long-term effects on attentional processes nearly 40 y after the episode, even with excellent long-term nutritional rehabilitation and independent of socioeconomic conditions in childhood and adolescence. This finding has major public health implications for populations exposed to early childhood malnutrition. *J. Nutr.* 142: 788–794, 2012.

## Introduction

Pre- and postnatal malnutrition affects not only the physical health but also the longer-term cognitive and behavioral development of affected children. Prenatal malnutrition is associated with behavioral morbidity, the full impact of which has only been recognized as outcomes are measured in adulthood (1,2). Adult survivors of the Dutch and Chinese famines exposed to prenatal malnutrition showed an increased prevalence of schizophrenia (3–5). Survivors of the Dutch famine are also reported to exhibit increased antisocial behaviors (6) and affective disorders (7,8). By contrast, the published data on adult outcomes after postnatal malnutrition are limited. Nutritional supplementation in the first 2 y of life in a chronically undernourished Guatemalan cohort was associated with im-

proved educational achievement and intellectual functioning at 30 y of age (9,10). Cognitive stimulation in early childhood was found to be more effective than nutritional supplementation, however, in improving the competence and intellectual outcomes of Jamaican adults with histories of childhood stunting (11). Other nutritional deficiencies in early childhood, including iron deficiency, have been associated with impaired neurocognitive functioning in young adults (12). Early nutritional deficits, including childhood stunting and iron deficiency, have also been associated with hyperactivity and attention deficits in childhood and adolescence (12–14). To our knowledge, however, there are no longer-term studies of the effects of childhood malnutrition on adult attention.

The BNS<sup>8</sup> is a 40-y longitudinal study whose goal is to evaluate the lifelong impact of an episode of postnatal malnutrition (15–21). Study participants had normal birth weight but subsequently experienced an episode of moderate to severe

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<sup>8</sup> Abbreviations used: ADHD, attention-deficit hyperactivity disorder; BNS, Barbados Nutrition Study; CAARS, Connors Adult ADHD Rating Scales; CPT, Continuous Performance Task; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders; T1, time 1; T2, time 2; T3, time 3.

protein-energy malnutrition, which was limited to the first year of life. They were identified as infants at the time of hospital admission and subsequently enrolled in a government-supported intervention program at the national Barbados Nutrition Centre until 12 y of age to ensure that there was no ongoing malnutrition after the infantile episode. The comparison group was selected in 1977 at the time of the first comprehensive assessment of this sample at age 5–11 y and consisted of healthy classmates who were matched to the index group by age, sex, and handedness. Studying the long-term effects of childhood malnutrition can be methodologically challenging because malnutrition typically coexists with poverty, infection, poor sanitation, maternal depression, crowding, and low birth weight, all of which present risks for child development. The BNS therefore collected detailed information pertaining to participants' social circumstances, which was considered in all group comparisons.

Although the index children showed complete catch-up in physical growth by the end of puberty (18), they displayed persisting cognitive deficits, including lower IQ (17) and poorer academic achievement (22), as well as impaired fine motor skills (16). Significantly, their teachers reported a striking 4-fold increase (60% vs. 15%) in the prevalence of attention problems relative to healthy comparison children (19,23,24). These attention problems, which predicted poor performance on a national high school entrance examination (15), were independent of IQ (19) and persisted through adolescence (24).

In the current study, we investigated whether these attention problems could still be detected in middle adulthood. We hypothesized that previously malnourished adults would exhibit an increased rate of attention deficits relative to the healthy comparison group and that this increase would not be accounted for by their cognitive impairment. Accordingly, the study addressed 2 main questions: 1) does the prevalence of attention symptoms differ between adults with histories of infant malnutrition and a healthy comparison group? and 2) to what extent are these attention problems associated with compromised cognitive abilities? We also explored whether attention problems observed in childhood would predict attention problems in adulthood. The primary focus of the study was to compare the prevalence of attention problems in previously malnourished adults with a healthy control group and not to assess the prevalence of ADHD as a psychiatric diagnosis.

## Participants and Methods

### Participants

All participants were born in Barbados, an English-speaking Caribbean country currently ranked 47 of 187 nations on the 2011 United Nations Development Programme Human Development Index (25). The majority of the population is of African origin and socioeconomically lower middle class, with a 99% literacy rate. Whereas malnutrition was common on the island when the participants were born, it has now been virtually eliminated.

Previously malnourished participants included every child born between 1967 and 1972 in Barbados who had been admitted to the Queen Elizabeth Hospital, Barbados, with a single episode of grade II–III protein-energy malnutrition (marasmus or kwashiorkor), based on the Gomez classification of expected weight for age (26). Additional inclusion criteria were as follows: normal birth weight, absence of pre- or postnatal complications, Apgar scores  $\geq 8$ , the absence of encephalopathic events during childhood, and no further malnutrition or serious medical illness after the initial episode. These children were hospitalized for ~6 wk during the first year of life and were subsequently enrolled in an intervention program at the Barbados Nutrition Centre, where they

were followed to 12 y of age. This government-supported program provided nutrition education; subsidized food, health care, and growth monitoring; and regular home visits by trained community health sisters (27). The recruitment process is described in detail elsewhere (15,18,23).

Individuals in the healthy comparison group had been matched as children for sex, age ( $\leq 3$  mo), and handedness to the index children at time of the first comprehensive assessment of this sample at age 5–11 y, and they met the same inclusion criteria. They had no histories of malnutrition or other serious childhood diseases at any time from birth through adolescence. Three healthy children from the same classroom as the index child were selected as potential matches, and birth and childhood health records were used to inform final selection of one healthy comparison child per index child.

### Design

Participants were assessed comprehensively at 3 time points spanning childhood and adolescence and as adults (Supplemental Fig. 1). In 1977 we evaluated 129 children with a history of marasmus and 129 healthy comparison children who were aged between 5 and 11 y at that time. The same children were reevaluated in 1982 (not shown in the Supplemental Fig. 1). In 1984 and again in 1991 (not shown), an additional group of children who had been hospitalized for kwashiorkor ( $n = 54$ ) during the same period as the marasmus children were recruited for comparison purposes. At these times, 124 (marasmus,  $n = 62$ ; healthy comparison,  $n = 62$ ) of the original 258 children were selected for evaluation because they were the best matches for age, sex, and grade in school to the kwashiorkor group. Note that the reduction in sample size at that point was not due to attrition but to a specific focus on potential differences in outcome between marasmus and kwashiorkor.

Between 2007 and 2010, 145 individuals from this cohort were again studied as adults. Although we were able to account for 98% of the original study participants, we were able to study only half of the original group because of limited funding to support recruitment and data collection. This attrition raised concerns about ascertainment bias. Participants and nonparticipants did not differ, however, in terms of the proportion of individuals who were malnourished compared with controls or their sex, age, childhood IQ, and household standard of living (Table 1). Thus, the adult participants appeared to be representative of the original participant group.

Informed consent was provided by all parents of the study participants when they were younger than 18 y under protocol E1962, approved by the Boston University Medical Center Institutional Review Board, and by the Ethics Committee of the Barbados Ministry of Health. Current oversight is provided by the Judge Baker Children's Center Human Research Review Committee (assurance no. FWA 00001811). All adult participants provided written informed consent.

### Measures

Measures obtained in adulthood included a self-report behavioral questionnaire (CAARS–Self-Report Screening Version), a laboratory measure (CPT), and a short-form IQ test. Other measures were obtained from BNS archival data obtained at T1, except for the standard of living measure for the kwashiorkor group, which was obtained at T3. Childhood rather than contemporary measures of household standard of living were used because current status was viewed as a potential outcome of long-term cognitive and behavioral impairment. CAARS scores were available for 143 (of 145) participants, and CPT scores were available for 136 (of 145) participants. Two participants had CPT scores but no CAARS scores.

**Adult measures (collected at 37–43 y of age).** CAARS Self-Report Screening Version (28). This 30-item scale yields 4 subscales based on DSM-IV criteria for ADHD symptoms: inattentive symptoms, hyperactive/impulsive symptoms, ADHD symptoms score (inattention + hyperactivity), and ADHD index, which includes the necessary items for the ADHD diagnosis of the DSM-IV. Each item is scored on a 4-point Likert scale (0 = not at all, 1 = just a little, 2 = pretty much, 3 = very much). The questionnaire was administered by a local interviewer because of the low reading levels of some participants. The CAARS has good internal consistency, test-retest reliability, and concurrent validity, ranging from

**TABLE 1** Characteristics in childhood of individuals who did or did not participate in the adult follow-up phase of the Barbados Nutrition Study<sup>1</sup>

	History of malnutrition		Healthy comparison	
	Participants	Nonparticipants	Participants	Nonparticipants
<i>n</i>	80	103	65	64
Male, <i>n</i> (%)	44 (55)	63 (61)	36 (55)	41 (64)
Age in 2010, <i>y</i>	40.4 ± 1.9	40.0 ± 2.0	40.0 ± 1.9	40.0 ± 1.9
Childhood IQ	91.6 ± 14.6	89.9 ± 16.6	105 ± 11.7	103 ± 13.4
Childhood standard of living factor	-0.9 ± 0.9	-1.0 ± 1.0	-0.3 ± 0.8	0.0 ± 0.9

<sup>1</sup> Values are means ± SD or *n* (%). There were no significant participation effects or a nutrition × participation interaction (ANOVA and logistic regression).

0.66 to 0.83 for adults (29). The CAARS also has good factor validity (28), and the inter-item correlations are in the expected directions and follow ordinal scaling properties. Although developed in the United States, the CAARS has been used in international studies (30). To ensure validity in Barbados, we performed principal components factor-extraction of all 30 CAARS items, followed by normal varimax rotation. Two factors, which accounted for 38% of the total variance, were selected for rotation. Their item content led us to interpret them as measuring inattention (factor 1; 17 items with factor loadings >0.45) and hyperactivity (factor 2; 5 items with factor loadings >0.45); Armor  $\theta$  values of 0.94 and 0.66, respectively, confirmed reliability. These results correspond to those from the published scale and confirm their psychometric properties in this setting.

**Conners CPT-II.** This standard, computer-based task (31) provides measures of reaction time, impulsivity, and vigilance and is relatively free of cultural bias, involving only the detection of letters. Primary outcome measures are as follows: omission (number of targets the participant fails to respond to) and commission errors (number of times the participant responds to a nontarget stimulus), reaction time, and reaction time SE (consistency of response time expressed in SE for responses to target). Twenty individuals (17 previously malnourished and 3 comparisons) obtained a T-score  $\geq 100$ , which is a signal of potential unreliability of the scores (32). Because the distribution of these scores was so imbalanced across the nutrition groups, we judged them to be potentially meaningful and therefore truncated all CPT scores >80 to a final value of 80 (~3 SD above the mean) before analysis rather than deleting these cases or using the unusually high scores (involving 28 participants). As a result, however, we could not use the Clinical Confidence Index, which is generated based on an algorithm that uses the omission error score. Published split-half reliabilities for the CPT scores range from 0.66 to 0.95, but test-retest reliability estimates range from 0.05 to 0.92, depending on the variable measured (31). Test-retest reliabilities are high, however, for composite ADHD indices (0.89) (31,33).

**Wechsler Abbreviated Scale of Intelligence.** Although we have previously reported on IQ in childhood and adolescence (15,17), contemporaneous IQ estimates were used in the current study because current cognitive level would be most likely to affect current performance on the attention measures. The short-form version (Vocabulary and Matrix Reasoning) of the Wechsler Abbreviated Scale of Intelligence (34) provided an estimate of full-scale IQ. Its internal consistency is excellent, with reliability coefficients ranging from 0.96 to 0.98 and with test-retest reliabilities ranging from 0.87 to 0.92 (35).

**Archival measures (collected at 5–18 y of age).** **Teacher Behavior Questionnaire, attention scale.** This scale was derived from a 30-item teacher questionnaire, modeled after one used by Richardson et al. (14) in Jamaica, which we administered when the participants were 5–11 y of age (23). Teachers were blind to the nutritional history of the children. Factor analysis showed a first principal component that appeared to represent attention (23) and was used as the attention scale (mean = 0, SD = 1); this factor showed high internal consistency (Cronbach  $\alpha$  = 0.92). In addition, we identified 2 items from the questionnaire, “pays attention” and “fidgety behavior,” that had high face validity as measures of attention for purposes of exploratory analysis. Because

participants who had kwashiorkor had not been recruited into the study until T3, these data were not available for those participants.

**Barbados Ecology Questionnaire.** A 50-item Socioeconomic and Ecology Questionnaire (36), adapted from a scale used in a similar population in Jamaica (14), assessed ecological conditions in the home, as well as educational level and employment history of the parents. This questionnaire was collected at 3 time points, when the children were aged 5–11, 9–15, and 11–17 y. Factor analyses of questionnaire items were applied separately at each time point (T1, T2, and T3) and subsequently combined because the factor structure and content across time points were comparable. Items that contributed most strongly to the derived factor reflect primarily the household standard of living (e.g., having or not having a refrigerator, bath, television, electricity, running water, closet, gas or electric cooking fuel; number of bedrooms; number of rooms; weekly household food expenditure; type of toilet; and weekly household income), which is a salient discriminator among Barbadian households. The reliability of this factor was  $\theta = 0.86$ . Factor scores were calculated separately at all 3 childhood time points, and all 3 scores were included in the longitudinal analysis comparing nutrition groups. Correlations of these scores across measurement points were large [T1–T2 ( $r = 0.72$ ); T2–T3 ( $r = 0.80$ ), and T1–T3 ( $r = 0.73$ ); all  $P < 0.0001$ ].

**Medical assessments.** All participants were evaluated using standard procedures. Nutritional status was assessed based on heights, weights, BMI, and laboratory measures (including hemoglobin, hematocrit, serum protein, globulin, ferritin, folate, and vitamin B-12 and the albumin:globulin ratio).

### Statistical methods

Data were analyzed by using SAS statistical software, version 9.2 (37). The distributions of all variables were first examined for approximate normality, followed by natural log transformation to reduce skewness of the CAARS and CPT data. Median values were compared by using Wilcoxon tests. Associations between CAARS and CPT scores and between childhood and adult measures were determined by using Spearman rank correlations. Longitudinal multiple regression analyses were applied (and implemented using Proc Mixed in SAS) to address the study aims, the effects of infant malnutrition, childhood household conditions (measured at T1, T2, and T3), and IQ as predictors of adult attention. These analyses involved simultaneously fitting separate multiple regression equations at T1, T2, and T3, thereby allowing the effects of childhood standard of living to vary over time. By simultaneously fitting these regressions, it was possible to formally evaluate how similar or different the effects were across time. Because the effects of childhood standard of living at each time period were found to be similar, a simplified regression was fit that pooled information regarding this variable from all 3 childhood periods. Finally, for inferences about the regression parameters, SEs were based on the empirical (or so-called sandwich) variance estimator, thereby accounting for the correlation among the errors in the 3 regression equations (arising from the fact that the same outcome, albeit different covariate values for childhood standard of living, appeared in the 3 regressions). Because individuals with histories of marasmus and kwashiorkor did not differ on any adult outcome, their data were combined. The significance level was set at  $P < 0.05$ , and we did not control for experiment-wise error.

## Results

**Participant characteristics.** Participants with histories of malnutrition came from less advantaged childhood homes, had less education, lower status jobs, and lower IQ scores than did the healthy comparison group (Table 2). Their heights, weights, BMI, and laboratory measures of nutritional status did not differ, however.

In terms of the primary outcomes, males had higher scores on the CAARS hyperactivity scale only ( $P < 0.05$ ), but there were no other sex differences. Childhood standard of living (36) was not associated with any of the CAARS or CPT scores. Correlations between representative CAARS and CPT scores ranged from 0.2 ( $P < 0.05$ ) to 0.3 ( $P < 0.001$ ).

**Effects of childhood malnutrition.** CAARS scores were consistently higher (indicating more attention problems) in the previously malnourished group. Moreover, using published clinical cutoffs (28), 6 of 80 (8%) of the previously malnourished participants (but none of the control participants) had scores exceeding the threshold for probable clinical diagnosis based on U.S. norms (T-score  $>65$ ). After adjustment for childhood standard of living, there were significant effects of malnutrition for the CAARS inattention scale, DSM-IV ADHD symptoms, and the ADHD index, with a trend-level difference ( $P = 0.05$ ) for the hyperactivity scale. Note that estimated regression coefficients of 0.10 to 0.15 for the malnutrition effect corresponded to ~10 to 15% relative differences between the means of the 2 groups (Table 3).

The groups also differed on the CPT. Fifty-three (69%) previously malnourished participants and 28 (47%) controls had at least one CPT score that fell within the clinical range for attention disorders (T-score  $>60$ ). Multiple regression analyses (adjusted for childhood standard of living) confirmed the significant effect of malnutrition on CPT performance. Participants in the previously malnourished group made more commission and omission errors and exhibited more variable reaction times.

**Role of IQ.** Because malnutrition is associated with decreased IQ (16), we also included adult IQ in the model to assess to what extent observed attention problems in adulthood might be

related to concurrent cognitive compromise (Table 3). IQ was generally not a significant independent predictor of CAARS scores; importantly, the magnitude of the malnutrition effect decreased only minimally with IQ in the model. The inclusion of IQ in the model attenuated the effect of malnutrition to a greater extent for the CPT, presumably reflecting the greater cognitive demands of this laboratory-based task. (Findings were similar when we corrected for childhood and adolescent IQ, as measured by the Wechsler Intelligence Scale for Children at the 3 time points).

**Correlation of attention symptoms in childhood and adulthood.** Associations between the teacher-rated attention measures at age 5–11 y (23) and the adult attention measures were necessarily limited to the marasmus group and their controls (Table 4). This was because early classroom measures had not been obtained for the kwashiorkor group, who were recruited into the study later. Teacher ratings (attention scale) were significantly correlated with all CAARS scores and with the CPT omission and commission errors and variability in reaction time. The “pay attention” item, which had the highest loading on the attention scale in the factor analysis, predicted the CPT scores and also the ADHD index on the CAARS. The “fidgety and unable to settle down” item, in contrast, predicted all of the CAARS scores, as well as CPT omission errors and reaction time variability. Thus, inattention in childhood predicted increased attention problems in adulthood.

## Discussion

Attention problems were elevated in adults who had suffered from childhood malnutrition 40 y earlier and who were subsequently nutritionally rehabilitated. These elevations were present in both males and females and were not accounted for by a childhood environmental disadvantage. Cognitive impairment in adulthood was closely associated with performance on the CPT, a laboratory-based measure of attention, but was only minimally associated with self-reported clinical attention problems on the CAARS, a behavior questionnaire. Thus, our primary hypothesis was largely confirmed: previously malnourished adults have an increased level of attention problems and, for self-reported problems, this increase was not accounted for by their cognitive impairment. Moreover, teacher-reported attention problems in childhood predicted adult attention problems, which is indicative of continuity across the life span.

We observed persistent effects of early malnutrition on attentional processes in these individuals in childhood (19,23,24) and now in adulthood. Moreover, we showed continuity: teacher observations on a questionnaire measure in grammar school were correlated with attention measures obtained in adulthood. The profile typically involved inattention to a greater extent than hyperactivity, and only individuals (8%) in the index group achieved a clinical diagnosis of attention deficit disorder based on published cutoffs. The continuity of attentional symptoms across the life span is also compelling.

The correspondence between laboratory and questionnaire measures of attention is well known to be only moderate, and the correlations in the current study are within the reported range (38). Of note, IQ did not predict CAARS scores but was significantly correlated with CPT performance. The present findings thus suggest that the CPT, like other laboratory measures of attention and executive functioning, is cognitively driven in contrast to questionnaire measures of behavior, which better reflect day-to-day functioning.

**TABLE 2** Selected characteristics of previously malnourished and healthy comparison groups<sup>1</sup>

	History of malnutrition	Healthy comparison	$\chi^2$ or Z	P-value
<i>n</i>	80	65		
Males, <i>n</i> (%)	45 (56)	35 (56)	0.01 <sup>2</sup>	0.93
Age in 2010, <i>y</i>	40.1 ± 2.2	39.6 ± 2.3	-1.20 <sup>3</sup>	0.23
Childhood standard of living factor	-0.9 ± 0.9	-0.3 ± 0.8	-3.52 <sup>3</sup>	<0.001
Hollingshead occupation (adult) score	5.7 ± 1.4	4.4 ± 1.7	-4.45 <sup>3</sup>	<0.001
Hollingshead education (adult) score	4.9 ± 0.6	4.2 ± 1.4	-4.05 <sup>3</sup>	<0.001
Estimated adult IQ (WASI <sup>4</sup> )	82.8 ± 16.6	99.0 ± 15.4	5.27 <sup>3</sup>	<0.001
Adult weight, <i>kg</i>	82.0 ± 17.0	81.0 ± 18.7	-0.55 <sup>3</sup>	0.58
Adult height, <i>cm</i>	169.3 ± 8.2	169.0 ± 8.0	-0.33 <sup>3</sup>	0.74
Adult BMI, <i>kg/m</i> <sup>2</sup>	28.6 ± 5.9	28.3 ± 6.0	-0.67 <sup>3</sup>	0.50
Adult hemoglobin, <i>g/L</i>	138 ± 16.5	135 ± 20.5	-0.85 <sup>3</sup>	0.39

<sup>1</sup> Values are means ± SD or *n* (%).

<sup>2</sup> Chi-square test

<sup>3</sup> Wilcoxon test.

<sup>4</sup> WASI, Wechsler Abbreviated Scale of Intelligence.

**TABLE 3** Unadjusted means and SD for log-transformed T-scores and parameter estimates for models assessing the effect of infant malnutrition adjusted for childhood standard of living with and without IQ<sup>1</sup>

	Unadjusted means $\pm$ SD		Malnutrition effect adjusted for childhood standard of living		Malnutrition effect adjusted for childhood standard of living and adult IQ	
	History of malnutrition	Healthy comparison	$\beta$	SE	$\beta$	SE
<b>CAARS</b>						
<i>n</i>	80	63				
Inattentive symptoms	3.7 $\pm$ 0.2	3.6 $\pm$ 0.1	0.10**	0.03	0.08*	0.04
Hyperactive symptoms <sup>2</sup>	3.7 $\pm$ 0.2	3.7 $\pm$ 0.1	0.06	0.03	0.06	0.03
DSM-IV ADHD symptoms	3.7 $\pm$ 0.2	3.6 $\pm$ 0.1	0.10**	0.03	0.09**	0.03
ADHD index	3.8 $\pm$ 0.2	3.7 $\pm$ 0.1	0.09**	0.03	0.06	0.03
<b>CPT</b>						
<i>n</i>	77	59				
Commission errors <sup>3</sup>	3.9 $\pm$ 0.2	3.8 $\pm$ 0.2	0.09*	0.04	0.07	0.04
Omission errors	4.1 $\pm$ 0.3	3.9 $\pm$ 0.2	0.12**	0.04	0.07	0.04
Reaction time	4.0 $\pm$ 0.2	4.0 $\pm$ 0.2	0.03	0.04	0.00	0.04
Reaction time SE	4.1 $\pm$ 0.3	3.9 $\pm$ 0.2	0.11*	0.05	0.08	0.05

<sup>1</sup> ADHD, attention-deficit hyperactivity disorder; CAARS, Connors Adult ADHD Rating Scales; CPT, Continuous Performance Task; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders. \* $P < 0.05$ , \*\* $P < 0.01$ .

<sup>2</sup> Sex effect ( $\beta = 0.06$ ,  $R^2 = 0.03$ ,  $F = 4.4$ ,  $P < 0.05$ ); males had a higher score.

<sup>3</sup> Sex effect ( $\beta = 0.08$ ,  $R^2 = 0.04$ ,  $F = 5.0$ ,  $P < 0.05$ ); females had a higher score.

These data are consistent with previous reports of persisting behavioral effects of childhood nutritional deficits through adolescence. In a long-term study in Jamaica, stunting in the first 2 y of life was associated with hyperactivity in late adolescence, an effect that was not reversed by supplementation or stimulation early in life nor accounted for by IQ (13). Other nutritional deficiencies, especially iron deficiency, are also known risk factors for attention problems in adolescents (12,39,40), but iron supplementation can reverse this deficit (41). In the current study, adult nutritional status was comparable for previously malnourished and comparison adults, and there was no evidence of iron deficiency in the adult participants. These data suggest that infant malnutrition results in permanent neurodevelopmental compromise, with attention symptoms being one prominent feature, in the absence of stunting or other evidence of ongoing nutritional deficits. Other factors that may lead to inattention were also considered but not found to play a role, including disadvantaged household conditions in childhood and medical disorders.

In the general population, childhood attention problems have implications for adult development (42,43). One 6-y follow-up study showed continuity between adolescent and young adult behavioral problems, including a strong predictive association between “pre-adult attention problems” and adult “irresponsibility” (44,45). Adults with ADHD, moreover, have more troubled educational histories and lower educational attainment, as well as an increased likelihood of dysthymia, alcohol and cannabis dependence/abuse, learning disorders, and psychological distress (46), possibly mediated by their compromised attention as children. We previously reported an increase in depressive symptoms (20,21) in the Barbados sample during childhood and adolescence, which were associated with cognitive and attention problems in childhood. Because the BNS is collecting extensive data on psychiatric and adaptive outcomes in adulthood, the potential mediating role of these more fundamental attentional processes in terms of long-term functional outcomes can be further examined.

The present study has several limitations. First, the adult sample included just under half of the participants identified in

**TABLE 4** Spearman rank correlations between teacher-reported attention ratings at age 5–11 y and adult CAARS and CPT scores for marasmus and healthy comparison groups combined ( $n = 118$ )<sup>1</sup>

	Teacher Behavior Questionnaire attention scale	How well does the child pay attention to you in class?	Is he/she usually fidgety and unable to settle down in the classroom?
<b>CAARS</b>			
Inattentive symptoms	0.21*	0.11	0.22*
Hyperactive symptoms	0.19*	0.12	0.26**
DSM-IV ADHD symptoms	0.20*	0.15	0.25**
ADHD index	0.23*	0.19*	0.24*
<b>CPT</b>			
Commission errors	0.19*	0.18	0.14
Omission errors	0.26**	0.19*	0.21*
Reaction time	0.14	0.09	0.19
Reaction time SE	0.26**	0.21*	0.27**

<sup>1</sup> ADHD, attention-deficit hyperactivity disorder; CAARS, Connors Adult ADHD Rating Scales; CPT, Continuous Performance Task; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders. \* $P < 0.05$ , \*\* $P < 0.01$ .

childhood, which raises questions about representativeness. We found no differences, however, between those who participated as adults and those who did not on key childhood measures. Second, our 2 primary attention measures have not been previously validated in Barbados. Factor analysis of the CAARS questionnaire items completed by our Barbados participants, however, yielded factors that aligned with the clinically relevant inattention and hyperactivity dimensions measured by the CAARS. Moreover, sex effects on the hyperactivity scale are in the expected direction, with higher scores reported in males, and teacher reports of key attention items correlated with CAARS and CPT scores 30 y later. Thus, the CAARS appears to be valid in the Barbadian setting. Third, we did not correct for multiple comparisons. Bonferroni corrections, however, which are a potential safeguard against type I errors, are well known to be overly conservative (47). Moreover, with 8 comparisons of CAARS and CPT scores, we would expect less than one significant result due to chance at the conventional  $\alpha = 0.05$  level. Thus, the numerous statistically significant effects of malnutrition reported in Table 3 are unlikely to be due to chance alone. Fourth, ~14% of participants had CPT omission scores in a potentially unreliable range. Although we took steps to address this issue analytically, the results nevertheless must be interpreted with caution.

Finally, the measures extracted from our archival data were designed specifically for this study during an era when the volume and diversity of well-standardized questionnaire measures that are now marketed were not available. Although their psychometric properties undoubtedly fall short by contemporary standards, the significant associations over time between these archival measures and contemporary measures of function support their validity. Moreover, the opportunity to examine attentional and other processes in a life span context is rare and likely outweighs any shortcomings of individual measures.

In conclusion, these findings have important implications for public policy, which has generally been directed at short-term medical solutions after significant malnutrition has occurred, such as improving growth and immediate physical effects. Given the lifelong functional compromise shown by our study, even among individuals whose medical management after the malnutrition episode was excellent, short-term investment in prevention may in the long run prove to be highly economical in view of the potential long-term social costs. It is equally important to monitor children who have survived early malnutrition, who will be at heightened risk as they reach adulthood. As more children survive infantile malnutrition, with improved access to medical care and rehabilitation, the lifelong consequences for behavior and mental health outcomes are of growing concern. These may become more prominent as this population ages, with implications for an intergenerational cycle of poverty and malnutrition.

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