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Early Childhood Malnutrition Predicts Depressive Symptoms at Ages 11–17

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Abstract

Background—We examined the prevalence of depressive symptoms in Barbadian youth with histories of infantile malnutrition and in a healthy comparison group and the extent to which the effect of malnutrition was mediated/moderated by maternal depression.

Methods—Depressive symptoms were assessed using a 20-item scale administered to youths (11–17 years of age) who had experienced an episode of protein-energy malnutrition (marasmus or kwashiorkor) during the first year of life and in a comparison group of healthy youths without a history of malnutrition. Their mothers completed the same questionnaire on the same test on three occasions when their children were 5–17 years of age at 2– 5 year intervals.

Results—The prevalence of depressive symptoms was elevated among previously malnourished youth relative to healthy comparison children ($p < .001$). When youth depression scores were subjected to a longitudinal multiple regression analyses, adjusting for the effect of maternal depressive symptoms, significant effects due to the history of early childhood malnutrition remained and were not discernibly attenuated from an unadjusted analysis. We also found significant independent effects of maternal depressive symptoms and age on youth depressive symptoms.

Conclusion—Early childhood malnutrition contributed independently to depressive symptoms in youths who experienced a significant episode of malnutrition in the first year of life. This relationship was not mediated or moderated by the effects of maternal depression. Whether the later vulnerability to depression is a direct effect of the episode of malnutrition and related conditions early in life or whether it is mediated by the more proximal neurobehavioral effects of the malnutrition remains to be determined.

Keywords

mood; depression; protein- energy malnutrition; kwashiorkor; adolescence

INTRODUCTION

Malnutrition early in life has been implicated in the subsequent development of cognitive and behavioral impairments in childhood and adolescence; decreased attention, conduct

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problems and decreased IQ have all been documented (Galler, 1984; Galler & Barrett, 2001; Walker, Chang, Powell, Simonoff, & Grantham-McGregor, 2006; 2007).Most published studies, however, have not been able to distinguish among the effects of low birth weight, chronic malnutrition and an acute episode of undernutrition during critical periods of brain and behavioral development.

This report is one of a series examining the long-term growth and development of Barbadian children with normal birth weights who had experienced a well-documented episode of marasmus, that is, moderate-severe malnutrition arising from the lack of protein, energy, and other nutrients, or kwashiorkor, a lack of protein only, which was limited to the first year of life. Since the index children were identified at the time of hospital admission, the episode was documented in detail. These previously malnourished children were compared to healthy classmates from the same neighborhoods who had never experienced malnutrition. The children were followed longitudinally into adolescence and are currently being evaluated as adults. In addition, at the time of the adolescent follow-up, an additional sample of children who had experienced kwashiorkor was included to determine whether these two conditions had similar or different effects. These children were selected to be comparable demographically to those who had experienced marasmus and their controls. The present report focuses on the longitudinal findings from marasmus group and their controls, but also includes cross-sectional findings from the kwashiorkor group for comparison purposes.

Prior reports on this sample documented that the previously malnourished youth from the marasmus and kwashiorkor groups demonstrated no evidence of continuing malnutrition after the early childhood exposure, with complete catch-up in physical growth by the end of puberty (Galler, Ramsey, Salt, & Archer, 1987a). Nonetheless, they exhibited persistent cognitive and behavioral deficits relative to peers without malnutrition histories (Galler et al., 1987b,c; Galler, Ramsey, Morley, Archer, & Salt, 1990; Galler & Barrett, 2001). Behavioral sequelae observed when the children were in grammar school included a four-fold increase in observed attention symptoms in the children with histories of malnutrition relative to controls (Galler, Ramsey, Solimano, & Lowell, 1983; Galler et al., 1990). These attention symptoms mediated the association between prior history of malnutrition and poor performance on a high school entrance examination at 11 years of age.

Perhaps significantly, when the children were of grammar school age, mothers of children with histories of malnutrition reported a higher prevalence of depressive symptoms than did mothers of comparison children (Salt, Galler, & Ramsey, 1988). Maternal depressive symptoms, moreover, were negatively correlated with children's reading scores and school performance. A similar, although more modest, relationship was found with the child's emotional stability and physical hygiene (appearance of cleanliness) as well as with marks in language arts (reading, writing and literature). These findings led us to speculate that maternal mood also contributes to the long-term behavioral and cognitive sequelae of early malnutrition. Mothers of children with early malnutrition reported elevated depressive symptoms relative to mothers of healthy comparison children at all observation times (Galler et al., in review). These depressive symptoms are of particular concern because of the significant risks posed by maternal depression for developmental outcomes (Beardslee, Versage, & Gladstone, 1998; England & Sim, 2009; Focht-Birkerts & Beardslee, 2000; Civic & Holt, 2000; Luoma et al., 2001; Chang, Halpern, & Kaufman, 2007; Halligan, Murray, & Cooper, 2007). Although major depression in mothers is a well understood risk for adolescent depression (Weissman et al., 2006; Pilowsky et al., 2006), data from several longitudinal studies indicate that chronic mild maternal depression can also raise the risk for depression in children and adolescents (Zuckerman & Beardslee, 1987; Chen, Johnston, Sheeber, & Leve, 2008; Hammen & Brennan, 2003; Hammen, Shih, & Brennan, 2004).

In addition to increasing the child's later risk for depression on the basis of associated maternal depression, early malnutrition may also increase risk on independent basis by having a direct impact on brain development. Low birth weight, an indicator of suboptimal growth conditions *in utero*, has been implicated in child and adolescent depression in epidemiologic studies in the United States (Costello, Worthman, Erkanli, & Angold, 2007) as well as in adults from the Dutch Famine cohort (Brown, van Os, Driessens, Hoek, & Susser, 2000). Although follow-up studies of children malnourished postnatally are limited, two recent reports from Jamaica did, however, confirm an association between growth stunting (linear growth retardation) that occurred between 9 and 24 months of age and increased symptoms of depression and low self-esteem in adolescents (Walker et al., 2006, 2007). The underlying biological mechanism which may explain the vulnerability of children with histories of malnutrition to develop depressive symptoms is poorly understood, although animal models of perinatal malnutrition have demonstrated certain outcomes which are also seen in animal models of depression, including altered HPA axis, impaired BDNF levels, and reduced numbers of neuronal cells (Galler, Shumsky, & Morgane, 1996, Aguilera et al., 2009).

Of note, the prevalence of depressive symptoms among mothers of the growth-stunted children was reduced among those who had participated in a program of psychological stimulation in early childhood (Walker et al., 2006). Moreover, mothers of children who participated in the intervention program themselves reported fewer depressive symptoms during that period than mothers of children in the untreated comparison group (Baker-Henningham, Powell, Walker, & Grantham-McGregor, 2005). Thus, in the clinical setting, the distinction between the direct impact of the malnutrition itself and the impact of elevated levels of depressive symptoms in mothers of previously malnourished children is problematic.

In order to clarify these issues, we evaluated the prevalence of depressive symptoms in our cohort at adolescence with specific reference to concurrent and prior history of depressive symptoms in mothers, using self-report instruments validated for use in Barbados (Salt et al., 1988; Galler, Harrison, Ramsey, Biggs, & Forde, 1999; Galler et al., 2004; Galler, Harrison, & Ramsey, 2006; Galler et al., in review). Adolescents with prior histories of both marasmus and kwashiorkor were included in the cross sectional analyses, but only those with marasmus could be included in the longitudinal analyses.

The study addressed two key questions: (1) Is the prevalence of depression symptoms elevated among youth with histories of malnutrition, and secondarily is there a difference between those with histories of marasmus and kwashiorkor; (2) To what extent is the association between childhood malnutrition and youth depressive symptoms mediated and/or moderated by maternal depressive symptoms? Because of the known associations between socioeconomic status and malnutrition on the one hand, and depressive symptoms on the other, family standard of living was adjusted for in the analysis. Our unique longitudinal database provides an opportunity for more detailed understanding of the antecedent conditions predicting and mediating the potential emergence of depressive symptoms in children and youth who suffered from significant malnutrition early in life.

METHODS

Description of Study

Site—The study was conducted in Barbados, a Caribbean country whose current population is approximately 260,000 persons. The composition of the population is 92% African/Caribbean origin, 4% Caucasian; the remaining population consists mainly of persons of Asian, Lebanese and Syrian descent. In 1970, the infant mortality rate was 46 per 1,000 live

births. Today that rate stands at 7.8 and Barbados is ranked as 31 on the Human Development Index (UNDP, 2007/8). Thus, whereas moderate-severe cases of infant malnutrition were of significant concern when this study was undertaken in the 1970's, infant malnutrition is now virtually eliminated from the island due to its improved economy and the impact of island-wide nutrition-related education (Ramsey, Demas, & Trotter, 1984; Ramsey, 2006).

Design and Participants—The data pertaining to this study were collected as part of a now 40 year longitudinal study of the long term effects of early malnutrition on behavior and development conducted at the National Nutrition Centre, Bridgetown, Barbados, in cooperation with the local Ministries of Health and Education. After the initial episode of malnutrition, the children were enrolled and followed at the National Nutrition Centre to 12 year of age, where they were part of a nutrition intervention program, providing regular medical visits and an educational program in nutrition, hygiene and parenting. All participants were documented as having good health and nutrition subsequent to their hospitalization. Referral to the Nutrition Centre was obligatory as part of a national effort to address malnutrition on the island, and all children on the island who were malnourished or were at risk for malnutrition were enrolled in the Centre's program.

Figure 1 illustrates the design. In 1977 (T1), all school-aged children participating in the National Nutrition Centre program and who had been hospitalized in their first year of life with a diagnosis of Grade II or III (Gomez scale) protein-energy malnutrition (marasmus) between 1967 and 1972 were invited to participate in the study (n=129). Three healthy children were selected from the same classrooms as each index child matched by sex, age (within 3 months) and handedness with that child, as potential comparison subjects. One of these three was ultimately selected based on availability of birth and early childhood records and adequate documentation of good health and growth (n=129). Inclusion criteria for both groups were normal birth weight, absence of pre- or post-natal complications, and no known neurological deficits. These index and control children were followed up in 1983 (T2). In 1985 (T3), 54 children, also followed by the Nutrition Centre, and who had been hospitalized during the same period for kwashiorkor were recruited, and their status was compared to that of 62 of the children from the marasmus group and 61 children from the healthy comparison group, resulting in a total N of 177. The marasmus and healthy comparison children were selected to participate in the T3 study because they were the best matches for age, sex and grade to the kwashiorkor group. Nine participants (6 marasmus, 2 kwashiorkor, and 1 healthy comparison) did not complete the morale scale that is the focus of this study, resulting in 168 participants evaluated in the present study, as detailed in Figure1.

Informed consent was provided by all families who participated in the study, under Protocol E1962, which was 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).

Measures

Youth and Maternal Mood Scales—Youth and maternal depressive symptoms were measured using the Minnesota General Adjustment and Morale Scale (Rundquist & Sletto, 1936). This 20-item scale was orally administered by a Barbadian psychologist and had an agree/disagree format (Salt et al., 1988; Galler et al., 1999; Galler et al., in review). This scale was judged to be the best instrument available for this cultural setting at the time the study was designed in the early 1970's. It has high internal consistency (Armor theta= 0.72)

and its concurrent validity with the Zung Depression and Anxiety Scales has been well documented in an independent sample of healthy Barbadian women (Galler et al., 1999; Galler, Harrison, Ramsey, Butler, & Forde, 2004 a; Galler et al., 2004 b; Galler et al., 2006).

Correlations among individual items on the scale were analyzed (separately for the youth and their mothers) by principal components factor-extraction (SAS Institute, Inc., 2006). We routinely exclude items with 90% or greater similar responses. However, all 20 items on the youth scale had sufficient variability and were included in these analyses. (Similar factor-structures emerged from analyses of phi-coefficients and their normalized counterparts (Comrey, 1975). Because loadings on the first rotated and unrotated factors were almost identical, and because the 2nd and 3rd rotated factors had relatively few items with high loadings, we preserved only the first unrotated factors for further analysis. Scale scores based on this factor were standardized to have zero mean and unit variance. Reliability of test scores was estimated using Armor theta, a measure of internal consistency similar to the Cronbach alpha (Armor, 1974). Table 1 lists items that contributed to the first unrotated principal component from the youth self-report morale scale (Armor theta = 0.64). This factor, which accounted for 13% of the total variance, appeared to reflect depressive symptoms, especially hopelessness. As described in a recent companion paper, we also computed a principal components analysis based on maternal data that were combined across the T1, T2 and T3 time points to allow for valid comparisons across time points. The first unrotated factor from the maternal scale also appeared to measure depressive symptoms; scores derived from this factor are used in the present report.

Socioeconomic and Ecological Factors—A Socioeconomic Status and Ecology Questionnaire assessed conditions in the home, as well as educational level and employment history of the parents. It was developed specifically for use in Barbados and was based on a scale used in a similar population in Jamaica (Richardson, 1974). The questionnaire contains 50 scoreable items assessing environmental conditions that were most relevant to the social context at the time (Galler, Ramsey, & Solimano, 1984; Galler & Ramsey, 1985; Galler, 1987; Galler, Harrison, Ramsey, Forde, & Butler, 2000). Factor analysis, again based on data combined across all three time points, identified a first principal component (theta = 0.86) that appeared to represent the household standard of living (Galler et al., unpublished). It was used as the indicator of socioeconomic status for this study. Scale scores based on this factor were standardized to have zero mean and unit variance. Specific demographic characteristics of the groups are summarized in Table 2. Relative to the comparison group, families of the malnourished children had lower income and more children in the home. Mothers were less well educated and had their first child at a younger age. Finally, the children were born later in the birth order. Thus, even though the comparison group was recruited from the same neighborhood and school, there were salient differences and controlling for these standard of living variables was important.

Statistical Methods

Two sets of multiple regression analyses (MRA) were applied to address the two research questions. The first set of MRAs, entering age, household standard of living and history of childhood malnutrition, tested whether previously malnourished children exhibit higher rates of depressive symptoms. The second set of MRAs, which tested the extent to which any differences between the marasmus and healthy comparison groups were mediated/moderated by maternal depressive symptoms, were performed entering age, standard of living, history of malnutrition and the maternal depressive symptoms score (and an interaction between history of malnutrition and maternal depressive symptoms score for the test of moderation). These MRAs were applied to our longitudinal database, which included marasmus and

healthy comparison groups, and were followed by a cross-sectional MRAs limited to T3, which included an additional nutrition group, kwashiorkor, who were assessed at T3 only.

The *longitudinal MRAs* (implemented using Proc Mixed in SAS) were performed, based on the longitudinal data on maternal depressive symptoms (at T1, T2 and T3) and standard of living (at T1, T2 and T3) that were available for the marasmus (n=56) and comparison (n=60) groups only (as shown in Table 3). These analyses involved simultaneously fitting separate multiple regression equations at T1, T2, and T3, thereby allowing the effects of maternal depression and 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 these effects were found to be similar at each time, a simplified regression was fit that pooled all of the information from all three occasions. Finally, for inferences about the regression parameters, standard errors were based on the empirical (or so-called "sandwich") variance estimator, thereby accounting for the correlation among the errors in the three regression equations (arising from the fact that the same outcome, albeit different covariate values, appeared in the three regressions).

The longitudinal analyses were followed by a complementary set of *cross-sectional MRAs*, based on the 168 subjects (see Figure I and footnote) who were evaluated at T3. Kwashiorkor and marasmus groups did not differ on any parameter and hence were combined for the T3 cross-sectional analyses . Only one item was missing and this was addressed by a mean substitution method, based on the time point, sex and malnutrition status of the child.

RESULTS

Associations between History of Malnutrition, Maternal Depressive Symptoms and Youth Depressive Symptoms

a. Longitudinal Analyses (Marasmus and Healthy Comparison Groups Only)— The primary question was whether the previously malnourished youths would exhibit elevated levels of depressive symptoms. Descriptive statistics that address this question are summarized in Table 3. Previously malnourished youth with histories of marasmus (who were assessed at T3 and whose parents were assessed at T1, T2 and T3) reported more depressive symptoms than did youth from the healthy comparison group, 0.30 versus −0.33. This effect of malnutrition on depressive symptoms corresponds to a difference of almost 2/3 of a standard deviation. Younger participants also reported more depressive symptoms than older youth ($r = -0.33$, $p<.001$), with similar levels of correlation within the previously malnourished group ($r = -0.34$; $p<.001$) and comparison group ($r = -0.34$; $p<.01$). Sex was not significantly associated with the youth depressive symptoms at ages 11–17, however. Table 3 also reports factor scores from the first unrotated principal component of the maternal morale scale (at T1, T2 and T3) and the household standard of living scales (at T1, T2 and T3).

Comparison of the marasmus and healthy comparison children (at T3) with those children who participated only at T1 or T2 revealed no differences in terms of age, sex, malnutrition status, maternal depression or standard of living scores. Hence, it was concluded that the smaller group studied at T3 (and serving as the basis for the longitudinal analysis) did not result in selection bias. Simple correlations indicated that higher maternal depression scores at T1, T2 and T3 each predicted higher youth depression scores at T3 (T1: $r = 0.29$; $p<.01$; T2: $r = 0.32$; $p<.001$; T3: $r=0.36$, $p<.001$). Household standard of living at T2 was significantly correlated with youth depressive symptoms at T3 ($r = -.25$; $p<.01$), but standard of living at T1 and T3 was only marginally correlated with youth depression at T3 (both $r = -.17$; $.1>p>.05$).

The relative roles of infantile malnutrition and maternal depression in predicting youth depressive symptoms were evaluated within a series of longitudinal multiple regression analyses that included age of the participant, malnutrition history, as well as maternal depressive symptoms and household standard of living over time (both at T1, T2 and T3) as predictors of youth depressive symptoms, along with relevant interaction terms. These analyses showed the independent effects of each predictor after correcting for the effects of the other predictors. To assess for the potential moderating effect of maternal depressive symptoms on the malnutrition effect, we also examined the interaction term for malnutrition with maternal depression. There was no significant interaction found. Thus, the interaction between malnutrition and maternal depression was eliminated from the final analyses reported below.

The results of a longitudinal MRA entering age, household standard of living (at T1, T2 and T3) and the history of malnutrition (but not including maternal depressive symptoms) show an estimated effect of malnutrition history to be 0.59 ($p<.001$), similar in magnitude to the unadjusted effect reported in Table 3. The results of a similar longitudinal MRA that, in addition, adjusts for the effects of maternal depressive symptoms, are displayed in Table 4. Of note, the estimated effect of malnutrition history, 0.53 ($p<.01$), in the latter analysis is only slightly attenuated from the effect reported above, and corresponds to a difference of approximately 1/2 of a standard deviation on the depressive symptoms scale. Overall, the relatively small attenuation of the malnutrition effect is consistent with a lack of a mediating effect of maternal depressive symptoms on this relationship. There were also significant unique effects of age ($p<.001$) and maternal depressive symptoms ($p<.001$) on youth depressive symptoms. The magnitude of the effect size for maternal depressive symptoms was 0.21. There were no effects of the household standard of living at any age after adjusting for the effects of the other variables in the model. Finally, because there were no significant effects of the demographic characteristics (mother's education, age at first pregnancy and birth order) shown in Table 2 to distinguish between nutrition groups, these were not retained in the final model.

b. Cross-sectional Analyses (Marasmus, Kwashiorkor and Healthy Comparison Groups)—These analyses were supplemented by an additional cross-sectional analysis at T3 which compared both groups of previously malnourished youth with the healthy comparison groups (n= 168). There were no significant differences in the level of depressive symptoms between the marasmus and kwashiorkor groups ($t=1.32$; $p=0.19$), whereas each index group did differ significantly from healthy comparisons (marasmus: $t= -3.48$, $p<.001$; kwashiorkor: $t= -2.08$, $p<.05$). Thus, the two previously malnourished groups were combined for the cross-sectional analyses. Because the kwashiorkor children were assessed only at T3, the analyses reported below controlled only for the T3 (concurrent) variables.

Fist, we examined the effects of childhood malnutrition on youth depressive symptoms. The MRA, entering age, household standard of living and malnutrition history, found an estimated effect of malnutrition history to be 0.46 ($p<.01$). In order to test the role of maternal depressive symptoms as a potential mediator of this effect, we performed a second MRA, entering age, household standard of living at T3, malnutrition history and concurrent maternal depressive symptoms at T3 as predictors of youth depressive symptoms. This analysis resulted in an adjusted multiple correlation for the cross-sectional analysis of youth depressive symptoms of 0.19 ($F=10.96$; $p<.0001$). Specifically, the adjusted effect of malnutrition history, 0.43 ($p<.01$), was qualitatively similar to the malnutrition effect reported above prior to correcting for maternal depressive symptoms. In this cross-sectional analysis there were also a significant unique effects of age, −0.21 ($p<.0001$) and maternal depressive symptoms, 0.19 ($p<.05$) but not for the household standard of living. Nor was the

interaction between malnutrition and maternal depression significant, confirming that there was no moderating effect of the maternal depressive symptoms on the malnutrition effect.

In summary, youth with histories of malnutrition endorsed more depressive symptoms than did the comparison group. Longitudinal analyses (based on the marasmus and comparison groups) confirmed that history of infantile malnutrition is an independent predictor of youth depressive symptoms, even after correcting for maternal depressive symptoms (which were independently associated with youth depressive symptoms). Although there was a small attenuation of the effect of malnutrition (a decrease of approximately 9% in the longitudinal model), importantly, maternal depressive symptoms did not function as either a mediator or moderator of the association between early malnutrition and youth depressive symptoms, and these associations were also independent of the effects of household standard of living. A supplemental cross-sectional analysis, which included an additional group of children with histories of kwashiorkor, similarly confirmed both elevated symptoms of depression as well as independent effects of malnutrition history (and maternal depressive symptoms). Within the previously malnourished groups, differences between children with histories of marasmus and those with histories of kwashiorkor were not statistically significant.

DISCUSSION

This study has two main findings. First, Barbadian youth with histories of early childhood malnutrition endorse a higher level of depressive symptoms than peers who did not experience such an episode. Second, maternal depressive symptoms, although more frequent in the mothers of previously malnourished youth, functioned as an additional independent predictor of youth depression symptoms, neither mediating nor moderating the association between malnutrition and youth depressive symptoms. The relationship between maternal depression and adolescent moods has been described in numerous populations (Weissman et al., 2006; Pilowsky et al., 2006; Hammen et al., 2003; Hammen et al., 2004; Chen et al., 2008), and our study confirms that this relationship was potent in Barbados as well. Although household standard of living was associated with youth depressive symptoms in simple correlations, it did not function as a predictor within the multivariate model (Table 4). Age, however, was a significant predictor with more depression among the younger subjects. This finding is consistent with the other reports of transient over-reporting of depressive and/or somatic symptoms in the junior high school age group (Radloff, L., 1991). Thus, our longitudinal data suggest that several independent and additive pathways lead to increased self-reports of depressive symptoms in previously malnourished youth.

Few studies have followed children with histories of early moderate-severe malnutrition into late adolescence and none other than ours has directly compared the long-term consequences of kwashiorkor and marasmus. The availability of a single population in whom both forms of malnutrition occurred in the first year of life could contribute to understanding the mechanisms underlying aberrant brain development in response to an early nutritional insult. The current study is consistent with our earlier reports from this Barbados series (Galler et al, 1987a,b,c; Galler et al, 1990) in confirming that the behavioral consequences of marasmus and kwashiorkor occurring at the same postnatal ages are comparable, suggesting that a nutritional insult during this critical period of brain development, irrespective of malnutrition type, is a key determinant of later risk for affective deficits.

The primary aim of this study, however, was to determine whether depressive symptoms are long-term sequelae of an early episode of malnutrition. Our results in fact corroborate those of Walker et al.(2006, 2007) in Jamaican adolescents with early growth failure, who had a higher prevalence of depression at 17 years of age. An earlier study in Jamaica (Richardson, et al, 1972) had reported that boys with histories of early malnutrition were unhappy at

school and were more likely to be withdrawn and solitary than their well-nourished classmates, suggesting that these children were also suffering from depressed mood. Although there is relatively little information available regarding postnatal malnutrition, prenatal growth retardation (which may be caused by maternal malnutrition) has been associated with an increase in adolescent depressive symptoms. A recent epidemiologic study of US children and adolescents with depressive symptoms in several counties in North Carolina found that low birth weight was associated with depression, primarily in girls (Costello, Worthman, Erkanli, & Angold, 2007). However, the prospective 1970 British Cohort Study confirmed that low birth weight predisposed to later depression at 26 years of age, though not at 16 years of age (Gale & Martyn, 2004).

Several longitudinal studies of populations exposed to prenatal malnutrition or with low birth weight have documented an increase in depressive symptoms in adulthood. The Dutch Famine Study confirmed an association between prenatal famine in the 2nd and 3rd semesters of pregnancy and major affective disorder in adult women (Brown et al., 2000). A 50- year Canadian study tracking neurodevelopmental antecedents of depression and anxiety over the life cycle found that heavier babies were less likely to experience depressive symptoms as they aged (Colman, Ploubidis, Wadsworth, Jones, & Croudace, 2007). A recent study of 1101 children from the US Perinatal Cohort (Vasiliadis, Gilman, & Buka, 2008), however, failed to detect a significant relationship between low birth weight and lifetime risk for major depression. Similarly, a long-term Finnish study did not document an association between low birth weight and the prevalence of depression at 31 years of age (Herva et al., 2008). Our study extends this literature to include the effects of early childhood malnutrition restricted to the first year of life.

The study has several limitations. One is the use of a non-standard depression scale. At the time this study was initiated, there were no hypotheses regarding the effects of malnutrition on depression. In the early 1970's, no other measures of depressive symptoms had been confirmed as being valid in the Barbados setting. Instead, our intention was to use a well-documented scale that had previously been used and validated as a measure of life adjustment and morale in relationship to economic hardships experienced in the 1930's. However, in another series of studies in Barbados using an independent sample of 229 healthy mothers and infants (Galler et al., 2004a,b; Galler et al., 2006), we were able to directly compare results from the General Adjustment and Morale Scale and the Zung Depression/Anxiety scales, and reported significant correlations between scores from the two instruments. Of note, many statements on the Morale Scale are identical or similar to questions contained in other mood scales and measures of self-esteem.

The limited role of household standard of living in the current study is somewhat surprising and also deserves comment. Household characteristics concurrent with the malnutrition episode were documented by us for the two malnourished groups, but this information was not available for the comparison group. Hence, the effects of household conditions may be underestimated. While socioeconomic circumstances of the households improved over time, especially between T1 and T2 (as shown in Table 3), the differences between previously malnourished and healthy comparison households remained constant. In other words, there was no interaction between test period and nutrition group. Moreover, we previously reported on the role of the microenvironment at T1 in school age children's functioning, when socioeconomic circumstances in the household were most disadvantaged (Galler & Ramsey, 1985). At that time, factors in the home environment and the early history of malnutrition were each independently and significantly associated with classroom behavior and IQ. However, further analysis of the individual components of the microenvironment revealed that maternal depressive symptoms were fully responsible for these effects (and no other aspect of the home environment played a role). Consistent with these earlier findings,

we again found no significant effects of household standard of living after adjusting for maternal depressive symptoms, suggesting that maternal depressive symptoms mediated the effects of the household socioeconomic circumstances.

The importance in understanding the interrelationships among early malnutrition, maternal depression and youth depression lies in the development of strategies aimed at alleviating the longer-term adverse effects of childhood malnutrition. Whether the later vulnerability to depression is a direct effect of the episode of malnutrition on neurodevelopment, associated home and family conditions at the time of the episode or whether it is mediated by its proximal neurobehavioral effects, such as compromised cognitive or attentional functions, remains to be determined. If the former is the case, intervention strategies should focus largely on facilitating cognitive development and alleviating the psychosocial impact of potential school impairment. If the latter, interventions targeted at the early identification of subclinical symptoms of depression would be advisable. Screening mothers and other primary caretakers for depressive symptoms could also be of relevance to improving the mental health outcomes of youths with a history of early malnutrition, since the prevalence of maternal depressive symptoms is likely elevated in this population and can further contribute to adverse child outcomes.

What's Known: Childhood malnutrition is associated with impaired cognitive and behavioral outcomes.

What's New: This study confirms that depressive symptoms are elevated in 11–17 year old youth with histories of malnutrition in the first year of life relative to healthy classmates. When youth depression scores were subjected to a longitudinal multiple regression analyses, significant effects due to malnutrition were found even after adjusting for the effect of maternal depressive symptoms. The malnutrition effect was neither mediated not moderated by maternal depression. However, we also found significant independent effects of maternal depressive symptoms on the prevalence of youth depressive symptoms.

What's Clinically Relevant: Youth with histories of early childhood malnutrition and their mothers should be screened for depressive symptoms. Addressing these clinical manifestations may have beneficial impact on the potential long term adverse consequences of early childhood malnutrition.

Abbreviations

PEM	protein-energy malnutrition
ANOVA	analysis of variance

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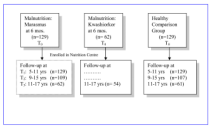

FIGURE 1. Research Design: Barbados Nutrition Study1

[1]Nine participants (6 marasmus, 2 kwashiorkor, and 1 healthy comparison) did not complete the morale scale resulting in a total of 168 participants in the present study.

TABLE 1

Items and Factor Loadings for First Unrotated Factor Derived from Principle Components Analysis of the Youth General Adjustment and Morale Scale (theta= 0.64) [1]

No one cares much about what happens to you	0.63
Success is more dependent on luck than real ability	0.60
Life is just a series of disappointments	0.58
Nobody appreciates me	0.51
Real friends are easy to find as ever	−0.49
Life is just one worry after another	0.45

[1] Only items with factor loadings at >.45 are presented. However, all 20 items from the morale scale were used to calculate theta and factor scores.

TABLE 2

Demographic characteristics of the study population (T_3).

	Marasmus (n=56)	Kwashiorkor (n=52)	Comparison (n=60)
Household Characteristics:			
Number of rooms	**4.39±1.01**	**4.46±1.13**	**4.70±0.95**
Number of children at home***	**3.72±1.74**	**5.43±5.30**	**3.10±1.62**
Weekly food costs ($Bdos)*	**$93.32±36.80**	**$89.55±37.36**	**$111.44±57.32**
Weekly income ($Bdos)**	**$142.90±64.20**	**$132.23±54.73**	**$171.95±79.73**
Natural father living in the home	**21.43**%	**28.85**%	**30.00**%
Maternal Characteristics:			
Mother's present health	**3.95±0.67**	**3.90±0.53**	**3.90±0.68**
Mother's years of school**	**9.00±1.38**	**8.79±1.14**	**9.60±1.59**
Mother's school performance	**1.95±0.75**	**1.96±0.68**	**2.18±0.60**
Age at first pregnancy*	**17.69±3.12**	**17.33±2.32**	**18.91±3.39**
Youth Characteristics:			
Child's age	**15.01±1.49**	**15.17±1.77**	**15.04±1.58**
Birth Order**	**2.48±1.54**	**2.14±1.08**	**1.72±1.04**

Effects associated with malnutrition history, F-test

* $p < 0.05$;

** $p < 0.01$;

*** $p < 0.001$

TABLE 3

Mean Factor Scores (SD) of Predictor and Outcome Variables by Nutrition Group and Measurement Period.

(Child's Age)	T_1 (4–11 yrs.)		T_2 (9–15 yrs.)		T_3 (11–17 yrs.)	
	Comparison	**Marasmus**	**Comparison**	**Marasmus**	**Comparison**	**Marasmus**
n	60	56	59	56	60	56
Youth Depression	---------	----------	----------	----------	−0.33	0.30***
Scores					(.98)	(1.01)
Maternal	−0.28	0.34**	−0.04	0.21	−0.13	0.15 ~
Depression Scores	(1.14)	(1.03)	(.87)	1.03)	(.95)	(.85)
Household	−0.25	−0.90***	0.74	0.22***	0.61	0.08***
Standard of Living	(.77)	(.89)	(75)	(.80)	(.68)	(.80)
Scores						

Effects associated with malnutrition history, t-tests:

~ 0.1>p>0.05

* p < 0.05;

** p < 0.01;

*** p < 0.001

TABLE 4

Longitudinal MRA of T3 Youth Depressive Symptoms, Reporting the Independent Effects of Postnatal Malnutrition (Marasmus) and Other Predictors (measured at T_1, T_2 and T_3)

Predictors	Regression Coefficient	Standard Error	t Value
Age (years)	−0.188	0.049	-3.88^{***}
Malnutrition	0.527	0.167	3.16^{**}
Maternal Depressive Symptoms	0.212	0.060	3.53^{***}
Household Standard of Living	−0.023	0.064	−0.35

** $p < 0.01$;

*** $p < 0.001$