Malnutrition at Age 3 Years and Lower Cognitive Ability at Age 11 Years

Independence From Psychosocial Adversity

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**Background:** Early malnutrition is linked to poor cognition, but long-term effects have not been extensively examined and psychosocial confounds have not always been controlled.

**Objective:** To test the hypothesis that malnutrition at age 3 years will be associated with poorer cognitive ability at age 11 years independent of psychosocial confounds.

**Design:** A prospective, longitudinal study of a birth cohort of 1559 children originally assessed at age 3 years for malnutrition (low hemoglobin level, angular stomatitis, kwashiorkor, and sparse, thin hair) and followed up to age 11 years.

**Setting and Participants:** A community sample of 1559 children (51.4% boys and 48.6% girls) born between September 1, 1969, and August 31, 1970, in 2 towns in the island of Mauritius, with 68.7% Indians and 25.7% Creoles (African origin).

**Main Outcome Measures:** Verbal and spatial ability measured at ages 3 and 11 years and reading, scholastic ability, and neuropsychologic performance measured at age 11 years.

**Results:** Malnourished children had poorer cognition at both ages. Deficits were stable across time, applied to all sex and ethnic groups, and remained after controlling for multiple measures of psychosocial adversity. Children with 3 indicators of malnutrition had a 15.3-point deficit in IQ at age 11 years.

**Conclusions:** Malnutrition at age 3 years is associated with poor cognition at age 11 years independent of psychosocial adversity. Promoting early childhood nutrition could enhance long-term cognitive development and school performance, especially in children with multiple nutritional deficits.

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**ARTICLE**

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An increasing body of evidence indicates a link between malnutrition and poor cognitive ability in children. In particular, there is growing evidence that early malnutrition could affect later cognitive function in childhood.1,3 Such prospective findings, which tease out temporal ordering of variables, suggest a causal relationship between poor nutrition and poor cognition. Such a model has received support from animals studies4,8 showing that early malnutrition affects brain structure and learning ability.

Despite such evidence, there is a question as to whether the nutrition-cognition link is confounded by psychosocial adversity. For example, several studies9,10 have found that controlling for psychosocial adversity attenuates or abolishes the malnutrition-IQ link. Nevertheless, some supplementation trials11 that control for the social environment still show beneficial effects of better nutrition on cognitive ability, although only a few studies9,12 have simultaneously controlled for multiple indicators of psychosocial adversity. One aim of this study is to assess whether the malnutrition-poor cognition relationship holds after controlling for general levels of psychosocial adversity. The more specific effect of parental education was also individually examined because some previous studies13 have found this variable to be particularly important.

A partial limitation of some longitudinal research on nutrition and cognition is that cognition is often measured at only 1 point, usually years after the nutritional assessment, but not at the time of nutritional assessment itself. Such studies have unanswered the question of whether the cognitive gap between malnourished and well-nourished children is static, decreases, or increases over time. The present study aims to address this issue by using measures of cognitive out-

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come at the time of nutrition assessment at age 3 years and again 8 years later at age 11 years.

Relatively few studies on cognitive ability have examined applied cognitive ability such as school performance and reading skills in addition to intelligence. If poor nutrition affects the ability to complete an IQ test but does not affect real-world issues such as school performance, then one could question the practical public health significance of nutrition-IQ relationships. The present study aims to address this issue by using measures of school performance and reading ability at age 11 years alongside IQ measures.

Human and animal studies have found that iron deficiency and protein-calorie malnutrition are associated with decreased cognitive functioning. On the other hand, the effects of several malnutrition indicators on cognitive deficits have not been extensively examined. Indeed, few previous studies assess more than 1 indicator of malnutrition. It is possible that a dose-response relationship exists such that children with multiple indicators of malnutrition have magnified cognitive deficits in later life. This study aims to examine this issue by using data from an existing longitudinal study to assess whether multiple indicators of malnutrition are associated with an increasing degree of cognitive impairment at age 11 years.

**METHODS**

**PARTICIPANTS**

Participants were obtained from a birth cohort of 1795 children from the island of Mauritius. All children born between September 1, 1969, and August 31, 1970, in 2 towns (Vacoas and Quatre Bornes) on the island were recruited into the study between September 1, 1972, and August 31, 1973, when aged 3 years. The 2 towns were chosen to be representative of the ethnic distribution of the whole island. The sample consisted of boys (51.4%) and girls (48.6%). Ethnic distribution was as follows: Indians, 68.7%; Creoles (African origin), 25.7%; and others (Chinese, English, and French), 5.6%. Census data for the island as a whole indicated 66% Indians, 29% Creoles, and 5% others, indicating that the study largely achieved its goal of sampling a population representative in sex and ethnicity. Following previous work on this population, data analyses were restricted to Indians and Creoles owing to the small sample size of the “other” ethnic category. Verbal informed consent was obtained from the mothers of the participants. Early research activities were conducted according to the principles outlined in the Declaration of Helsinki, which prevailed in 1972 when the research was initiated and did not require informed consent to be written, whereas research activities in later years were conducted using principles outlined in the Belmont Report. Institutional review board approval for retrospective data analyses was obtained from the University of Southern California and from the University of California, Los Angeles.

**CHILDHOOD NUTRITION DEFICITS AT AGE 3 YEARS**

The following 4 signs of malnutrition were assessed in an examination conducted by pediatricians of 1559 of the children:

1. Angular stomatitis: Cracking of the lips and corners of the mouth is predominantly a sign of riboflavin deficiency (vitamin B2), but it also reflects niacin and retinol (vitamin A) deficiency. The base rate for angular stomatitis in the sample was 7.0%.

2. Kwashiorkor: This condition, also known as protein malnutrition, is found in tropical regions and is common in children weaned on a high starch–low protein diet. Kwashiorkor is also an indicator of zinc and copper deficiency. The term means “red hair” in African dialect, after the classic symptom of this condition, which consists of a reddish orange discoloration of the hair. The base rate for red hair in the sample was 6.8%.

3. Sparse, thin hair: This is a sign of protein-energy malnutrition in particular and of malnutrition in general. Protein starvation leads to the cessation of hair growth, and zinc and iron deficiency can also lead to thin hair. The base rate for this symptom in the sample was 5.8%.

4. Anemia: Anemia was indicated by a low hemoglobin level, which reflects iron deficiency. Hemoglobin levels were assessed from a laboratory test of blood samples drawn from the child. Anemia was defined as a hemoglobin level below 8.5 g/dL. This definition of anemia was consistent with the medical practice in Mauritius in the early 1970s. The base rate of anemia in this sample was 17.0%.

Patients were defined as having nutritional deficits if at least 1 of these 4 indicators was present (22.6% of the sample); the control group consisted of individuals with no indicator present and was viewed as relatively better nourished (77.4% of the sample). To assess for a dose-response relationship between the number of indicators of malnutrition and verbal-spatial ability, participants on whom IQ data were available were categorized into 1 of 4 groups: no malnutrition (n=950 at age 3 years and n=837 at age 11 years), 1 indicator of malnutrition (n=180 at age 3 years and n=189 at age 11 years), 2 indicators (n=48 at age 3 years and n=51 at age 11 years), and 3 indicators (n=15 at age 3 years and n=13 at age 11 years). Because only 2 individuals had all 4 nutrition indicators across both ages, both were retained in the 3 indicators category. Children with significant medical problems of any kind (including malnutrition, scabies, and parasitic worm) were referred to appropriate agencies for treatment, but neither these clinical diagnoses nor the treatment outcomes were recorded or coded.

**INTELLIGENCE AND COGNITIVE ABILITY AT AGES 3 AND 11 YEARS**

**Age 3 Years**

Measures of verbal, spatial, and total cognitive ability were derived from 6 subtests of the Boehm Test of Basic Concepts–Preschool Version, which assesses basic verbal and visuospatial concepts that are fundamental for early school achievement. Full details of measurement, factor structure, reliability, and validity are given by Raine et al and Boehm. Data were available on 1260 participants.

**Age 11 Years**

Estimates of verbal IQ (VIQ), performance IQ (PIQ), and full-scale IQ were assessed at age 11 years using 7 subtests of the Wechsler Intelligence Scale for Children. The similarities and digit span subtests formed an estimate of VIQ, and the block design, object assembly, coding, mazes, and picture completion subtests formed an estimate of PIQ. Data were available on 1385 participants for these 3 measures of IQ.
Scholastic Ability

Scholastic ability was based on scores on 4 standardized academic tests (English, French, mathematics, and environmental studies) given to all 11-year-old children throughout the country. Scores on these tests (graded 0-5) were summed to form an overall index of scholastic ability.19,20 Data were available on 1415 participants.

Reading Ability

Reading ability was assessed using the Holborn Reading Scale.22 This word recognition test consisted of 33 sentences of increasing difficulty. Total scores (number of sentences correctly read) were standardized into reading quotients.19,20 Data were available on 1263 participants.

Neuropsychologic Ability

Neuropsychologic test ability was assessed using the Trail-Making Test.33,34 The 2 components of this task (A and B) assess visuomotor tracking, motor speed, and attention, with Trails B also containing a working memory component.35 Time-to-completion scores for each component were corrected for age by residualization of scores (mean=0, SD=1).19,20 Data were available for Trails A on 1238 participants and for Trails B on 1156 participants.

PSYCHOSOCIAL ADVERSITY AT AGES 3 AND 11 YEARS

The psychosocial adversity index at age 3 years was based on 9 variables collected by social workers who visited the homes of the children at age 3 years (see Raine et al12,19 for full details). The index was created along lines similar to those described by Rutter26 in 1978 and Moffitt17 in 1990. A total adversity score was created by adding 1 point for each of the following 9 variables: father uneducated, mother uneducated, semiskilled or unskilled occupation, single-parent status, separation from parents, large family size, poor health of mother, teenaged mother, and overcrowded home. Complete data for this variable were available on 1793 of the children at age 3 years.

The psychosocial adversity index at age 11 years was based on 14 variables collected by social workers who visited the homes of the children at age 11 years. A total adversity score was created by adding 1 point for each of the following 14 variables: living in rented accommodations, living in a house without electricity or water, child has neither good toys nor good books, no television, living in poor housing, father uneducated, mother uneducated, parent psychiatrically ill, parent physically ill, teenaged mother (19 years or younger when child was born), single-parent status, separation from both parents, 5 or more siblings, and overcrowded home (≥5 family members per house room). Complete data were available on 1272 participants.

RESULTS

For all analyses herein, full-scale cognitive ability (the summation of verbal and spatial indicators) was not entered into MANOVAs to avoid multicollinearity, but to illustrate findings results report 1-way ANOVA comparisons for these indicators at ages 3 and 11 years.

COGNITIVE ABILITY AT AGE 3 YEARS

Effect of Malnutrition

Mean (SD) scores (and results of specific t test comparisons) for cognitive measures at age 3 years for the malnourished and control groups are given in Table 1. Malnourished children had decreased verbal but not spatial ability at age 3 years. A MANOVA conducted on verbal and spatial ability showed a main effect of group (malnourished vs control) (F2,1190=9.31; P<.001), indicating overall reduced cognitive ability at age 3 years in the malnourished group. There was a significant main group effect for verbal ability in the same direction (F1,1191=18.32; P<.001) but not for spatial ability (F1,1191=1.63; P=.20).

Potential Confounds

Malnourished children were more likely to experience psychosocial adversity than were control children at age 3 years (t1553=4.18), and they also had a less-educated mother (t=3.34) and a less-educated father (t=3.4) than controls at age 3 years (P<.001 for all). Consequently, it is possible that psychosocial adversity and parents’ edu-
The effects of malnutrition were further explored using multiple regression and MANOVA analyses. Significant effects were observed for several cognitive and psychosocial outcomes. For instance, malnourished children showed decreased Verbal IQ (F(2,1149) = 4.1; P = .006) and Full-scale IQ (F(2,1149) = 4.1; P = .006) compared to the control group. Similarly, the Trail-Making Test (Trails A and B) also showed significant differences between the groups (F(2,1149) = 4.1; P = .006) and (F(2,1149) = 4.1; P = .006), indicating decreased cognitive flexibility in the malnourished group.

The study also found that the confounding effects of psychosocial adversity were not significant when controlling for education level, as shown by the MANOVA results where the main effects of malnutrition remained significant even after adjusting for these confounders. The effect of malnutrition on cognitive outcomes was robust, even after controlling for other factors such as ethnicity and socioeconomic status.

To summarize, the study's findings suggest that malnutrition in early childhood has lasting effects on cognitive development, which persist into adolescence. Preventive strategies targeting malnutrition in early childhood are crucial to mitigate these long-term cognitive and psychosocial impacts.
Effect Moderators

There were no moderator effects for sex ($F_{4,934}=0.36; P=.84$) or ethnicity ($F_{4,897}=0.849; P=.49$) when these constructs were entered into the MANOVA as factors alongside malnutrition grouping.

IQ ACROSS CHILDHOOD FROM AGES 3 TO 11 YEARS

Because the effects of malnutrition described herein at age 3 years ($n=1193$) are based on a different sample from that used at age 11 years ($n=871$), it can be questioned whether the same results would be obtained when using exactly the same sample size across the 2 ages. Furthermore, one goal of the study was to assess whether cognitive deficits remained stable, increased, or decreased over time. This possibility was tested by conducting repeated-measures MANOVAs on each of verbal, spatial, and total cognitive ability, with time (age 3 or 11 years) as the repeated measure. Results showed significant main effects of the malnutrition grouping on verbal ability ($F_{3,1086}=11.45; P<.001$) and total cognitive ability ($F_{3,1086}=8.27; P=.004$), indicating reduced performance across both ages in malnourished children (Figure 1). The main effect of malnutrition on spatial ability was not statistically significant ($F_{3,1086}=2.92; P=.09$). No other main effects or interactions with time were significant.

DOSE-RESPONSE RELATIONSHIP

To assess for a dose-response relationship between the number of indicators of malnutrition and cognitive ability, MANOVAs (with 4 groups: 0, 1, 2, or 3 malnutrition indicators) were conducted on cognitive measures at ages 3 and 11 years (Figure 2). Results show a significant main effect for number of indicators on cognitive ability at age 3 years ($F_{3,2175}=4.50$) and at age 11 years ($F_{3,2175}=6.59$) ($P<.001$ for both). Significant group effects on univariate F tests were observed for verbal ability ($F_{3,1185}=6.53; P<.001$), spatial ability ($F_{3,1185}=3.31; P=.02$), and total cognitive ability ($F_{3,1185}=6.04; P<.001$) at age 3 years and for VIQ ($F_{3,1086}=8.52$), PIQ ($F_{3,1086}=10.98$), and full-scale IQ ($F_{3,1086}=12.14$) ($P<.001$ for all) at age 11 years.

INDIVIDUAL COMPONENTS OF MALNUTRITION

Results of MANOVAs and follow-up univariate ANOVA conducted on each of the 4 malnutrition indicators for cognitive measures at ages 3 and 11 years are given in Table 2. Results showed that low hemoglobin level was most strongly and consistently related to poor cognition at both ages. The MANOVAs indicated that angular stomatitis and kwashiorkor were also significantly related to cognitive indicators at age 11 years, but kwashiorkor was not related to cognition at age 3 years. Finally, sparse, thin hair was related to cognitive indicators at age 3 years but not at age 11 years.

COMMENT

The key findings from this study are that malnutrition at age 3 years is associated with poorer verbal and full-scale cognitive ability at age 3 years and poorer VIQ, spatial IQ, full-scale IQ, reading ability, and school and neuropsychologic performance at age 11 years. Critically, the deficits remained after controlling for up to 14 psychosocial adversity variables at age 11 years. Furthermore, the study showed significant dose-response relationships between the number of indicators of malnutrition and the extent of cognitive deficits at age 11 years, indicating that children who have more indicators of malnutrition are more likely to have lower cognitive ability. In addition, cognitive deficits in the malnourished group remained stable over time and were as strong at age 11 years as at age 3 years. Finally, the effect of malnutrition on later cognitive deficits did not differ between boys and girls or Indians and Creoles, as indicated by a failure of these measures to significantly moderate the group effect of malnutrition. Findings support the view that early childhood malnutrition is a potential risk factor for later cognitive deficits and, from a pediatric perspective, raise the possibility that promoting early childhood nutrition could enhance children’s long-term cognitive development and school performance.

Some previous studies\(^\text{9,16,38}\) argue that the malnutrition-IQ link is abolished after controlling for psychosocial and environmental confounds, whereas other studies\(^\text{10,39}\) that control for these confounds have been criticized for not adequately controlling for diverse psychosocial...
and environmental confounds. To better address this issue, this study took into account 9 different psychosocial deficits at age 3 years and 14 psychosocial deficits at age 11 years in assessing the relationship between nutritional status at age 3 years and cognitive status at age 11 years, as well as testing for the individual effect of parental education. Results remained significant for all analyses. These results suggest that nutritional deficits cannot easily be explained by psychosocial deficits, and they strengthen the case for nutritional deficits playing a direct role in shaping cognitive functioning. Nevertheless, we caution that other variables that are not controlled for such as prenatal factors (eg, low birth weight) could still play a role in predisposing to poor cognition and malnutrition.16,38

The robustness of the malnutrition–poor cognition link is exemplified with reference to 4 factors: type of cognitive outcome, sex, ethnicity, and repeated time points. Three different forms of cognitive functioning—standardized intelligence and concept formation, neuropsychologic ability, and school performance—were all shown to be poorer in malnourished children. These effects applied to boys and girls and to Indians and Creoles, indicating that malnutrition effects are invariant to sex and ethnicity. Furthermore, this study establishes that cognitive deficits are in place at an early age and 8 years later. The fact that the same results are found for different cognitive measures, time points, and groups suggests, but does not prove, that early malnutrition predisposes to cognitive deficits.

Some previous studies on early malnutrition and later cognition examined only a single nutrition indicator (eg, iron deficits only). Although use of multiple indicators has been strongly advocated,40 few studies have implemented this recommendation. In addressing this issue, it was found that the number of malnutrition indicators (0, 1, 2, or 3) present was strongly associated with the degree of cognitive deficit. For example, total IQ at age 11 years decreased by 3.3 points with 1 indicator present, 9.0 points with 2 indicators, and 15.3 points with 3 indicators (Figure 2). This dose-response relationship not only further supports the view that malnutrition pre-
disposes to poor cognition but also indicates that children with multiple nutritional deficits are increasingly handicapped and could especially benefit from targeted intervention. However, these new findings require further replication and extension before practical applications are drawn.

Previous studies have been criticized for not assessing indicators of micronutrients in addition to protein-energy malnutrition. In our study, we attempted to address this issue by analyzing 4 individual indicators of malnutrition. Results indicated that low hemoglobin level was most strongly and consistently related to poor cognition at both ages, with the exception of spatial ability at age 3 years (Table 2). The finding that low iron level (as measured by hemoglobin) was the only indicator related to all 3 forms of cognition at both ages is consistent with experimental studies in humans claiming beneficial effects of iron supplements on cognition in children, although several findings have been mixed, for example, those of Pollitt et al. Furthermore, experimental animal studies indicate that iron is involved in DNA synthesis, neurotransmitter production and function, brain myelination, and cerebellar white matter formation. On the other hand, the strength of the findings for hemoglobin may be because this was the most common indicator of malnutrition and increased statistical power for this analysis. Nevertheless, these findings further support the consideration of iron supplementation in future intervention research on cognitive functioning, although other indicators of malnutrition should not be discounted.

Kwashiorkor was also less strongly, but nevertheless significantly, related to cognition at age 11 years, whereas sparse, thin hair was linked to cognition at age 3 years. These 2 indicators reflect protein and zinc deficiencies, deficits that have been shown in animal studies to affect enzymes involved in neurotransmission, DNA, RNA, and protein synthesis and essential amino acids during brain development. Furthermore, rats fed a low-protein diet show reduced brain weight and low forebrain DNA concentrations, whereas diets reduced in zinc produce reductions in whole brain, hippocampus, and cerebral weight. It is possible, therefore, that low protein and zinc levels are factors that help account for the relationship between malnutrition and poor cognition in humans.

Angular stomatitis, an indicator of predominantly vitamin B2 deficiency (but also vitamin A) was significantly related to cognition at ages 3 and 11 years, although not as strongly as for hemoglobin level (Table 2). Although clear links have been established between vitamin A and cognition, to our knowledge, no previous study has examined the relationship between vitamin B2 deficiency and childhood cognition. The exact mechanism relating vitamin B2 (riboflavin) deficiency to cognition is currently unknown. However, it is known that riboflavin enhances the hematologic response to iron, and, consequently, riboflavin deficiency may result in iron deficiency and affect cognition through the same routes as for hemoglobin.

There are several limitations to the study that should be acknowledged. First, because malnutrition was assessed at age 3 years only, we cannot ascertain whether the cause of poor cognitive ability at age 11 years is due to malnutrition only in the first 3 years, when brain development reaches a critical stage, or whether it is produced by sustained malnutrition throughout childhood. Second, the conservative definition of anemia could result in some individuals in the control group having mild levels of malnutrition rather than having good nutrition, a fact that would underestimate the true strength of the relationship obtained between malnutrition and cognition. Third, not all children could be followed up to age 11 years, and slightly more Indians than Creoles were represented, although the results did not show ethnicity to be an effect moderator.

In conclusion, this prospective longitudinal study conducted on a large sample that included 4 indicators of malnutrition and 3 cognitive measures assessed 8 years apart showed malnutrition at age 3 years to be related to poor cognitive ability at ages 3 and 11 years. These findings applied to boys and girls and to all ethnic groups, and remained after controlling for 14 measures of psychosocial adversity. A dose-response relationship was observed between malnutrition and cognition, with children with several indicators of malnutrition having a 15.3-point deficit in IQ at age 11 years. Findings suggest that better attention to nutrition could have significant implications for cognitive development in children and adolescents.

**What This Study Adds**

Previous studies have shown that malnutrition is related to poor cognitive ability in children. However, few prospective longitudinal studies controlled for multiple indicators of psychosocial adversity, measured several malnutrition indicators, assessed multiple cognitive measures across time, and assessed for a dose-response relationship between malnutrition and IQ.

Results show that children with malnutrition at age 3 years have lower verbal and spatial cognitive ability at ages 3 and 11 years. These deficits were stable across time, applied to boys and girls and to all ethnic groups, and remained after controlling for 14 measures of psychosocial adversity. A dose-response relationship was observed between malnutrition and cognition, with children with several indicators of malnutrition having a 15.3-point deficit in IQ at age 11 years. Findings suggest that better attention to nutrition could have significant implications for cognitive development in children and adolescents.

**CONCLUSIONS**

In conclusion, this prospective longitudinal study conducted on a large sample that included 4 indicators of malnutrition and 3 cognitive measures assessed 8 years apart showed malnutrition at age 3 years to be related to poor cognitive ability at ages 3 and 11 years. These findings applied to boys and girls and to Indians and Creoles. Controlling for up to 14 indicators of psychosocial adversity did not abolish the malnutrition–poor cognition relationship. Children with 3 indicators of malnutrition had a 15.3-point deficit in IQ at age 11 years. Findings suggest that promoting early childhood nutrition could enhance long-term cognitive development and school performance, especially in children with multiple nutritional deficits. The fact that cognitive deficits are not only important in their own right but also contribute to public mental health problems such as schizophrenia, depression, and violence highlights the central importance of a full understanding of the role of malnutrition in relation to poor cognition and mental health status.

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