Central somatosensory conduction time in severely growth-stunted children[1–3]

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ABSTRACT To examine the effects of chronic malnutrition on central nervous system function, we used the somatosensory evoked potential to measure the central conduction time of 20 children aged 7-8 y with heights below the third percentile for their age and 20 control children in Honduras. The two groups differed significantly in socioeconomic status, achievement in Bender's neurointegrative test, and hematocrit, but not in birth weight. After median nerve stimulation, the mean central conduction time (interpeak latency between N13 and N20) for the growth-stunted group (6.19 ± 0.52 ms) did not differ significantly from that of the control subjects (6.30 ± 0.58 ms), suggesting appropriate myelination and fiber diameter. Somatosensory tracts may escape damage resulting from postnatal dietary deficiencies because myelination in these tracts is almost complete at birth. *Am J Clin Nutr* 1998;67:93–6.

KEY WORDS Malnutrition, stunted growth, somatosensory evoked potentials, somatosensory tracts, myelin, central conduction time, children

INTRODUCTION

The World Health Organization estimates that ≈230 million children worldwide have a low height-for-age, also called growth stunting (1). Height-for-age reflects long-term growth and is altered by chronic nutritional disorders. In Honduras, national surveys indicate that ≈33.9% of children aged < 5 y suffer from growth stunting (1), suggesting a pervasive effect of chronic malnutrition.

Central nervous system (CNS) injuries caused by severe malnutrition can be shown clinically through neurologic signs and symptoms such as dullness, apathy, irritability, muscular weakness and wasting, anxiety, chronic fatigue, hypotonia, hypo- or hyperactivity, attention deficit, and poor school performance (2). In addition to the clinical manifestations observed, electrophysiologic abnormalities have been detected in malnourished children. Changes have been observed in peripheral nerve conduction velocity (3) and brainstem auditory evoked potentials in children with marasmus and kwashiorkor, the most severe forms of acute malnutrition (4, 5). Relatively little is known about the adverse effects of chronic malnutrition on CNS physiology in humans.

There is evidence that the myelination process is impaired in malnourished children and animals. In humans, decreased concentrations of proteolipids, cerebroside, sulfatide, and plasmalogen were found in white matter as well as abnormal cellularity in different CNS sites. Extensive data from rats suggest a severe reduction in the brain myelin concentration due to malnutrition (6). Nevertheless, few studies have assessed the effects of malnutrition on the function of a long myelinated central tract in children.

Somatosensory evoked potentials (SSEPs) constitute a standard clinical technique used to assess the function of the somatosensory peripheral tracts and central projections. A peripheral nerve is stimulated transcutaneously and the propagated volley is recorded over peripheral and central structures, giving rise to well-characterized components. The cervical potential, reflecting postsynaptic activity in the cervical cord, is a negative wave with a latency of ≈13 ms (N13). The cortical component (N20) is generated by activation of the primary cortical somatosensory receiving area. Central conduction time can thus be measured by using the interpeak latency between the cervical N13 and the cortical N20, which represents the time necessary for nervous conduction between the cervical cord and the primary somatosensory receiving area (7). We compared the N13-N20 interpeak latency between growth-stunted (malnourished) and control children to assess the effects of chronic malnutrition on central nervous conduction.

SUBJECTS AND METHODS

A group of 20 growth-stunted children with heights below the third percentile for their age and 20 age- and sex-matched control subjects with normal heights were included in the study. The mean (± SD) ages of the control and growth-stunted groups were 7.4 ± 0.3 and 7.6 ± 0.4 y, respectively, and there were 7 girls and 13 boys in each group. The children were contacted through a family dental center where they were being treated. Parents signed informed consent forms, as required by the Ministry of Health in Honduras. Growth stunting was determined by using

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height-for-age charts provided by the Institute of Nutrition of Central America and Panama. Children with a history of neurologic pathology, neonatal hypoxia, convulsive syndrome, head trauma, or a low intelligence quotient were excluded. The study was conducted with the approval of the Department of Physiology of the National Autonomous University of Honduras.

A complete physical examination was performed by a physician (M-FR) and a blood sample was taken to determine hematocrit. A psychologist (ID) evaluated the children's intelligence quotient and determined their neurointegrative maturity using Bender's test normalized for Honduras (8). Bender's test is an extensively used psychologic exam in which nine figures are presented to a child and he or she is then asked to copy them. The ability of the child to reproduce the figures is determined by sensory motor actions that vary according to the intellectual maturity of the individual, ability to discriminate spatial position, and symmetry of graphic stimuli. The results can be classified for different levels (scored from 1 to 3) of visuomotor integration according to age. The lower the index, the better the achievement. Each child's mother completed a socioeconomic survey, and a socioeconomic status from 1 to 6 was assigned to each child on the basis of housing conditions, education, and occupation of the head of the household. A lower score indicated a higher socioeconomic status.

Recordings were made while the subjects were seated comfortably in a room with standard light conditions. The children were stimulated with a Grass S8 stimulator (Grass Medical Instruments, Quincy, MA) over the median nerve at the wrist with surface cup electrodes. Stimuli were 0.3 ms in duration and were delivered at a rate of 2–3 Hz at a voltage sufficient to produce a just-visible abduction of the thumb. Central conduction time was measured as the interpeak latency between the cervical N13 and the cortical N20 components of the SSEP. The cervical N13 and cortical N20 waves were recorded over positions C5S-EPc and CPc-Ac (10–20 International System), respectively, by using standard electroencephalogram cup electrodes with an electrolytic gel. Signals were amplified with a preamplifier (RPS 107; Grass Medical Instruments) and filtered passively with a bandpass of 10-10 000 Hz. Signals were digitized (MacAdios 8ain; GW Instruments, Medford, MA) and passed to a Macintosh computer (Cupertino, CA), where 1000 waves were averaged with SUPERSCOPE software (GW Instruments). The poststimulus analysis time was 40 ms. A minimum of two replicated waves (< 1% peak latency variation) was required. Impedances of the stimulating and recording electrodes were < 2 kohm, as measured in a sample of the subjects (n = 9).

Nonparametric data were compared statistically between the two groups with the Mann-Whitney U test and parametric data by analysis of variance with Scheffé post hoc comparisons. STATWORKS (Cricket Software Inc, Philadelphia) was used for the analyses.

RESULTS

The control and growth-stunted groups differed significantly in height, weight, visuomotor integration, hematocrit, and socioeconomic status, but not in birth weight (**Table 1**). A representative example of the SSEP for a control child is shown in **Figure 1**. We observed no significant difference in central conduction time between control and growth-stunted children. The mean (± SD) central conduction times of the control and growth-stunted children were 6.30 ± 0.58 and 6.19 ± 0.52 ms (**Figure 2**).

TABLE 1
Subject characteristics[1]

Variable	Control children	Growth stunted children
Height (cm)	121.07 ± 4.47	106.78 ± 3.91[2]
Weight (kg)	24.39 ± 3.61	18.44 ± 1.89[2]
Bender Test score	1.41 ± 0.64	2.76 ± 0.45[2]
Socioeconomic status	2.16 ± 0.00	4.80 ± 0.46[2]
Hematocrit	0.3931 ± 0.0237	0.3756 ± 0.0292[3]
Birth weight (kg)	3.41 ± 0.44	3.50 ± 1.22

[1] $\bar{x}$ ± SD.
[2,3] Significantly different from control children: [2] $P < 0.001$, [3] $P < 0.05$.

DISCUSSION

We carried out the first study of central conduction time in a somatosensory pathway in chronically malnourished children. The growth-stunted children in our sample had a mild but significant decrease in hematocrit, indicating a deficit in hemoglobin, which is usually associated with protein-energy malnutrition (9). Central conduction time in the growth-stunted children did not differ significantly from that in the control children. Central conduction time between the cervical cord and the primary somatosensory cortex involves transmission through *1*) the cuneate and anterolateral fasciculi, *2*) the medial lemniscus and the spinothalamic fibers to the ventral posterior nucleus of the thalamus, and *3*) thalamic radiations to primary somatosensory cortex. The normal conduction times we observed suggest that the fiber diameter and myelination of these tracts were not affected by malnutrition severely enough to induce growth stunting or to lower hematocrit values. Although no conduction deficit was observed with median nerve stimulation, there was the possibility that tibial nerve stimulation might have shown an

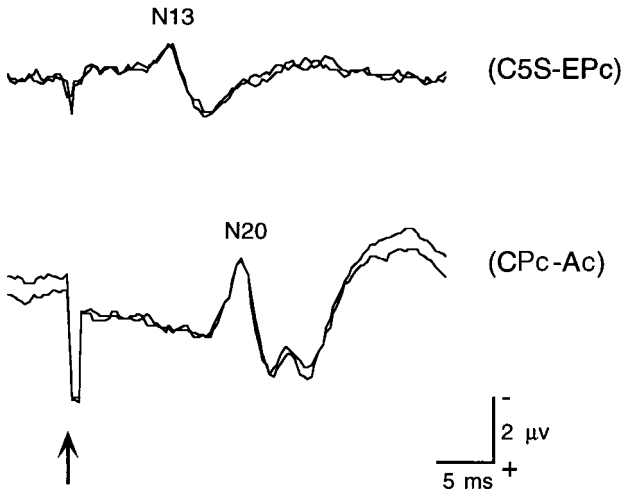

FIGURE 1. Representative traces showing the N13 and N20 waves of the somatosensory evoked potentials recorded simultaneously at positions C5S-EPc and CPc-Ac, respectively, in a control child. Each trace is an average of 1000. Shock artifact begins at the arrow.

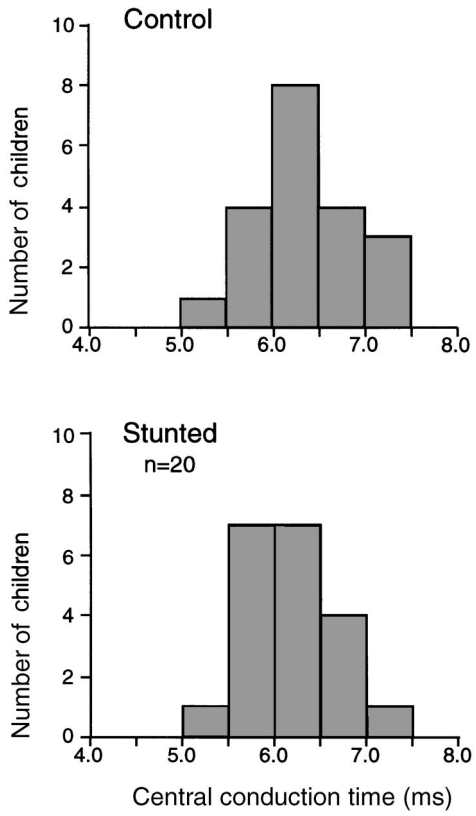

FIGURE 2. Histograms showing the distribution of central conduction time measured as the interpeak latency between the N13 and N20 potentials of the somatosensory evoked potential for control and growth-stunted children. There were no significant differences.

effect due to the increased conduction distance. This was unlikely, however, given that there was no trend toward longer conduction times in our medial nerve data. Nevertheless, future studies might examine the effects of malnutrition on tibial SSEPs as well as the possible differences between spinal and brain components of the pathway.

Our findings appear to support the notion (based largely on brain weight) that the developing CNS may be "spared" during times of nutritional stress (10). The simplest explanation of our findings, however, may relate to the critical periods of development of the tracts in question. All experts in this area agree that myelination of the different tracts takes place at different times and at different rates during development. Yakovlev and Lecours (11) described these variations as myelogenetic cycles (other authors have used the term myelinative phases). Tracts that acquire large amounts of myelin over a short developmental time have short myelinative phases and those that acquire large amounts of myelin over a prolonged time have long myelinative phases. For example, the medial longitudinal fasciculus and the cuneate fasciculus show early myelination and rapid myelinative phases. Myelination of the solitary tracts and cervical corticospinal tracts indicate slow progression from birth to the second postnatal year. Sites with long myelinative phases could be at greater risk of impairment over a greater portion of gestation and postnatal life. The medial longitudinal fasciculus in the human fetus is the first to undergo myelination early in the second half of gestation, followed by the afferent tracts, such as the cuneate fasciculus, gracile fasciculus, medial lemniscus, and lateral lemniscus (12). The normal birth weights of the stunted children in our study suggest that the nutritional insult was largely postnatal, thereby sparing the rapid, mostly prenatal, myelination of the somatosensory tracts. Myelination in the motor tracts and cerebrum mostly start at late gestation and progress well after birth (12).

Corticospinal fibers may have been at risk in the sample of children in the present study, as suggested by their impaired visuomotor skills. In rats, early postnatal malnutrition reduced the number of myelinated fibers in the corticospinal tract but not in the cuneate fasciculus (13). A previous study from our laboratory showed decreased conduction velocity of corticospinal fibers in adult rats that were malnourished postnatally during the first 3 wk of life (14). Other studies showed slowed conduction in auditory (15) and visual (16) systems of malnourished rats. Thus, the normal function we observed in the somatosensory system may not apply to other systems, especially those that mature postnatally and have long myelinative phases, such as the corticospinal tract.

Many previous studies showed altered neuropsychologic functions in malnourished children (17). An organic injury is thus suspected and may involve subtle changes in dendritic structure and synaptic function (17), in addition to altered nerve conduction. More human and animal studies are needed to adequately assess the neurologic effects of chronic malnutrition and its potential cost to society.

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