

Improved iodine status is associated with improved mental performance of schoolchildren in Benin¹⁻³

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ABSTRACT

Background: An adequate iodine supply in utero and shortly after birth is known to be crucial to an individual's physical and mental development. The question of whether iodine supplementation later in life can exert a favorable influence on the mental performance of iodine-deficient populations was addressed in various studies, but with contradictory results.

Objective: The aim of this study was to examine the effect of an improvement in iodine status on mental and psychomotor performance of schoolchildren (7–11 y) who were moderately to severely iodine deficient.

Design: The study, which was originally planned as a double-blind, randomized, placebo-controlled intervention, was carried out in an iodine-deficient population of schoolchildren ($n = 196$) in northern Benin. As the population began to have access to iodized salt during the 1-y intervention period, the study population was split post hoc—on the basis of urinary iodine concentrations—into a group with improved iodine status and a group with unchanged iodine status. Changes in mental and psychomotor performance over the intervention period were compared.

Results: Children with increased urinary iodine concentrations had a significantly greater increase in performance on the combination of mental tests than did the group with no change in urinary iodine concentrations.

Conclusions: An improvement in iodine status, rather than iodine status itself, determined mental performance in this population, which was initially iodine deficient. These findings suggest a “catch-up” effect in terms of mental performance. *Am J Clin Nutr* 2000;72:1179–85.

KEY WORDS Iodine deficiency, mental performance, schoolchildren, urinary iodine concentration, Benin, West Africa

INTRODUCTION

The public health importance of an adequate iodine supply for the physical and mental well-being of humankind has been well described (1, 2). Most studies on the relation between iodine status and mental performance of children have concentrated on effects of iodine supply in utero and shortly after birth on mental and psychomotor development (3–7). The most commonly held premise is that the mental capacity of children, once affected by iodine deficiency in early life, is impaired permanently. Few intervention studies have been carried out to examine whether

mental and psychomotor performance of growing children, while iodine deficient, may still benefit from iodine supplementation. In a double-blind, placebo-controlled study that examined the effect of iodine supplementation on the mental performance of children aged 5.5–12 y, Bautista et al (8) found no difference between supplemented and nonsupplemented children. In a double-blind, placebo-controlled intervention study in Malawi, iodine supplementation significantly improved the performance of 6–8-y-old children on many mental tests (9).

The purpose of this study was to determine whether the findings in Malawi could be confirmed in a different setting and, if so, to examine which specific aspects of cognitive functioning are influenced most by supplementation. The research was planned as a double-blind, randomized, placebo-controlled study involving oral doses of iodized oil in schoolchildren in an iodine-deficient area in northern Benin, West Africa. However, much earlier than expected—halfway through the intervention period—iodized salt was introduced into the study area. As iodine became available to both groups, the hypothesis that iodine supplementation improves mental performance could no longer be tested. Therefore, we tested whether children whose iodine status improved over the intervention period showed a greater improvement in mental and psychomotor performance than did children whose iodine status changed to a limited extent or not at all.

SUBJECTS AND METHODS

Study area and subjects

The study was carried out in the district of Basila, province of Atacora, in northern Benin, where prevalence rates of goiter

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in schoolchildren aged 6–12 y varied from 20% to 60% (A Doh, EA Ategbo, unpublished observations, 1994). The population, mostly Anii, was engaged in subsistence farming, with cotton as the sole source of cash income. Food security was a seasonal concern. Polygamy was common and households were made up of extended families. The 4 study villages had neither electricity nor clean drinking water.

Children aged 7–11 y from standards (grades) 2 and 3 in the 4 primary schools in the study area were considered for enrollment. In 2 of these 4 grades, all female children had been given an iodized oil supplement in the previous year; therefore, only boys were selected from these 2 schools.

The study was approved by the health and education authorities of the province of Atacora and by the Medical Ethics Committee, Division of Human Nutrition and Epidemiology, Wageningen University. The aim of the study was explained to local administrative and traditional authorities, parents, and teachers. After verbal approval was obtained from local authorities, the parents of the children, and the parent-teacher association, all children selected were examined physically by a clinician. Several children with skin or respiratory infections and malaria were treated. No children were excluded on health grounds.

Study design

Children were stratified by school, school class, and sex and subsequently were matched on the basis of similar age and height-for-age. From each pair of children, one child was randomly allocated to 1 of 2 groups. The groups were then randomly allocated to receive iodine supplements or a placebo. The study was double blind, randomized, and placebo controlled with the codes being broken only after completion of the final test. Iodized oil (Lipiodol UF 7; 540 g I/L) and the placebo (poppy-seed oil) were provided by Guerbet Laboratories (Aulnay-sous-Bois, France). Iodized oil and poppy-seed oil were dispensed as a single dose (1.0 mL) administered orally with a Swift 7 dispenser (English Glass Company, Leicester, United Kingdom) in January 1996.

Baseline anthropometric measurements were made and urine and blood samples were collected in October and November 1995. Baseline mental development tests were performed during the same period. All measurements and tests were repeated in October and November 1996. Additional urine samples were collected 1 wk and 5 mo after supplementation.

Somatic and biochemical indicators

Anthropometric measurements were made in duplicate. Height was measured to the nearest millimeter with a microtoise (Stanley Tools, Besançon, France). Weight was measured to the nearest 0.25 kg with a spring scale. Venous blood was drawn from the antecubital vein; one drop of whole blood was then immediately applied to a filter paper card (grade 903; Schleicher and Schuell, Keene, NH). These cards were air-dried for 1–2 h and packed in polyethylene bags before being frozen. Hemoglobin was assessed by using a Hemocue (Helsingborg, Sweden). Serum samples were prepared and frozen before being transported. Samples of urine (\approx 25 mL), to which some crystals of thymol were added, were collected. Blood-spot cards and frozen samples of urine and serum were transported to the Micronutrient Research Laboratory, University of Ghana at Legon, Accra, for analysis of urinary iodine [chloric acid digestion followed by the Sandell-Kolthoff reaction (10)], thyroid-stimulating hormone (TSH) in blood spots (SpectraScreen Dried Blood TSH EIA Kit;

IEM Diagnostica, Reflex Industries, Santee, CA), and serum ferritin (enzyme-linked immunosorbent assay) within the next 6–9 mo. Frozen serum samples were also transported to the Laboratory for Endocrinology, Amsterdam Medical Centre, Netherlands, for assessment of thyroglobulin (radioimmunoassay), free thyroxine (T_4) with time-resolved fluoroimmunoassay (Delfia; Wallac Oy, Turku, Finland), and TSH with an immunoluminometric assay (Brahms Diagnostica GmbH, Berlin).

Mental and psychomotor development tests

Because no comprehensive battery of mental tests has been developed for use in French-speaking West Africa, many tests consisting of nonverbal and abstract pictorial material from the French Kaufman ABC test battery (11) were pretested in a nearby village. Apart from the sequential memory test (hand movements), most tests contained images unknown to the children. Subsequently, a battery of tests, mostly nonverbal, was composed, which have been used under conditions comparable with those found in rural Benin (ie, tests requiring little or no vocabulary skills of the child being tested, thus avoiding confounding by education-related language skills). These tests covered, as much as possible, aspects of fluid intelligence, as opposed to crystallized intelligence (12–14). Fluid intelligence is regarded as one of the major constituents of intelligence; it refers to the ability to reason by analogy, to apprehend an unfamiliar configuration, and to construct or extract a solution. Crystallized intelligence refers to subject-matter proficiency acquired in the past, which is reflected in results of tests measuring such aspects as vocabulary, arithmetic, or factual knowledge. The mental test battery included the following 8 tests: block design (15), 5 tests (closure, concentration, exclusion, fluency, and mazes) from the African Child Intelligence Test (16), hand movements (11), and colored progressive matrixes (17). These tests, including the mental ability tested in each according to factors reported by Thurstone (18) and Ekstrom et al (19), are described in **Table 1**. In addition, 2 psychomotor tests—pegboard and ball throwing—were carried out. A psychologist (NB) trained 2 university graduates and 2 teachers from Benin to conduct the tests, which were subsequently pretested among schoolchildren from the study area who were not included in the study population. The testers worked in pairs. All 4 testers started with the same 3 tests in a fixed sequence. The remaining tests were administered by either one tester or the other, with the same tester always being responsible for the same set of tests. All children were given a snack before testing, which took place between 0900 and 1200 in a room that was quiet and free of distractions. The 8 mental tests plus the pegboard test took \approx 50–60 min, after which the children were taken outside for the ball-throwing test. Because of the diversity and short duration of the tests, children did not become tired or bored. A simple reaction-time test and a choice reaction-time test, both measuring information processing time, as well as a tapping test measuring manual dexterity and accuracy were administered at the end of the intervention period but not on the same day as the mental tests.

Data analysis

Data analysis was related to the modified study design. Children were allocated to new groups on the basis of the magnitude of change in urinary iodine concentration over the intervention period. Differences in changes in mental performance between these groups were assessed by using Student's *t* test. If not nor-



TABLE 1
Mental development tests used in the study

Test name	Test description	Mental ability tested
Block design, WPPSI (15)	With a set of colored blocks (2 colors; blocks having 1 or a combination of both colors), the tester arranges the blocks in a given design, after which the blocks are reshuffled and the child is asked to arrange the blocks in the same design within a specified time period.	Space ¹ , spatial orientation ² , memory (partly)
African Child Intelligence Test (16)		
Closure	A series of 35 test pages, each with one incomplete drawing of an everyday object, is shown to the child; for each test page, the child is asked to identify the incomplete figure within a specified time period, a task requiring mental reconstruction of what is missing.	Perception ¹ and speed of closure ²
Concentration	A set of 2 pages is covered with small circles with an oblong dark "eye" in 1 of 8 positions. The child is shown 1 example and is then asked to find and tick circles with the eye in the same position as in the example as quickly as possible, working line by line within a specified time period.	Perception ¹ and perceptual speed ²
Exclusion	A series of 30 test pages, each with 4 abstract figures, is shown to the child; from each test page the child is asked to choose 1 figure that lacks a common characteristic of the other 3.	Reasoning ¹ and induction ²
Fluency	In 2 fixed time periods, the child is asked to mention the first names of as many people as possible and, subsequently, the names of as many animals as possible.	Word fluency ^{1,2}
Mazes	The child is presented with a series of mazes in relief and asked to go with a small pointer through the maze as quickly as possible, while not being allowed to lift the pointer from the surface.	Space ¹ and spatial scanning ²
Hand movements, Kaufman ABC (11)	The child is asked to imitate a series of hand movements made by the instructor on a table; movements are specified and composed of 3 basic elements in varying sequence and number: the fist, the side of the hand, and the palm of the hand.	Sequential memory
Colored progressive matrixes, Raven test (17) ³	The child is presented with a series of colored, figural, rectangular pictures, out of which a small section has been cut. In addition, the child is presented with 6 different pictures that all have the form, size, and colors of the piece that was cut from the larger picture and is then asked which of the smaller pictures should be inserted into the larger one to make it complete again.	General ability and reasoning by analogy

¹On the basis of factors according to Thurstone (18). "Space" refers to the ability to accurately perceive spatial patterns and to compare them with each other.

²On the basis of factors according to Ekstrom et al (19).

³Sets A, Ab, and B used.

mally distributed, log transformations were made. Factor analysis, based on the intercorrelation of the tests, was carried out by using a principal components analysis with VARIMAX, an orthogonal factor rotation method. This enabled us to examine the construct validity of the test battery. All data were processed and analyzed by using SPSS-PC software (version 6.1 for WINDOWS; SPSS Inc, Chicago). Anthropometric indexes were calculated by using EPI-INFO (version 6.02; Centers for Disease Control and Prevention, Atlanta).

RESULTS

Initially, 211 children were enrolled in the study; 13 children left school or moved out of the area by the end of the intervention period and 2 children could not be located during urine collection. The socioeconomic status of the families included in the studies was generally poor. Families were large, landholding size was relatively small, and education levels among adults were low (Table 2).

Nutritional status

Thirty-three percent of the children were stunted [height-for-age < -2 SD of the National Center for Health Statistics (NCHS) reference; 20], 17% had low weight-for-age (< -2 SD of the NCHS reference), and 2% were wasted (weight-for-height < -2 SD of the NCHS reference) (Table 2). The proportion of

children with anemia (hemoglobin < 110 g/L) was 33%, whereas 11% had moderately to severely depleted iron stores (serum ferritin concentration < 18 µg/L). With an initial median urinary iodine concentration of 0.16 µmol/L (20.6 µg/L), the study population was classified as moderately to severely iodine deficient. At the end of the intervention period, both the original placebo and the iodine-supplemented groups showed clearly improved iodine status. However, the total study population was still classified as mildly iodine deficient on the basis of median urinary iodine concentrations. The initial urinary iodine concentration was positively correlated (Spearman) with the serum concentration of free T₄ ($r = 0.19$, $P = 0.007$) and negatively correlated with serum concentrations of thyroglobulin ($r = -0.51$, $P = 0.000$) and TSH ($r = -0.34$, $P = 0.000$). At the end of the study, the urinary iodine concentration was related to the serum thyroglobulin concentration only ($r = -0.21$, $P = 0.003$).

Mental performance

Correlations between the scores on the different tests at baseline were mostly positive (Table 3), in line with what is usually found (21). Factor analysis of the series of tests carried out by using VARIMAX produced 3 factors: block design, closure, concentration, exclusion, fluency, and maze tests loaded on one factor; the hand movements test loaded on the second factor; and the colored progressive matrixes, or Raven test, loaded on the third factor (Table 4). This pattern is similar to the pattern found

TABLE 2
General characteristics of subjects and their families

	Improved group		Unchanged group	
	Initial	Final	Initial	Final
Characteristics of subjects				
<i>n</i> (M:F)	—	128 (109:19)	—	68 (58:10)
Supplemented:nonsupplemented	—	68:60	—	29:39
Age (y)	9.1 ± 1.2 ¹	10.1 ± 1.2	8.5 ± 1.2	9.5 ± 1.2
Height-for-age <i>z</i> score	-1.73 ± 0.91	-1.70 ± 0.87	-1.48 ± 1.04	-1.43 ± 1.01
Weight-for-age <i>z</i> score	-1.35 ± 0.70	-1.38 ± 0.70	-1.32 ± 0.77	-1.33 ± 0.75
Education (y)	2.8 ± 0.9	—	2.6 ± 0.7	—
Characteristics of family				
Family size (<i>n</i>)	14.2 ± 7.2	—	14.8 ± 8.4	—
Education of parents (y)				
Father	1.3 ± 0.8	—	1.4 ± 0.9	—
Mother	1.2 ± 0.5	—	1.3 ± 0.8	—
Size of landholding (m ²)	31 000 ± 24 000	—	32 000 ± 27 000	—

¹ $\bar{x} \pm SD$.

in a study that used an intelligence test for Dutch, Spanish, and Indian children, and to that found when this battery of tests was compared with the Wechsler Intelligence Scale for Children-Revised (22–24). The first factor refers to spatial and perceptual reasoning skills, the second factor to sequential memory, and the third factor to general intelligence, often referred to as *g* (21, 25). The overall changes in performance over the intervention period were small but positive. The test-retest correlation of the full test battery in the unchanged group was 0.83 ($P = 0.000$).

Mental performance in relation to iodine status

Children were categorized both at the beginning and at the end of the study with respect to their urinary iodine concentrations (Table 5): normal-mild (>0.40 μmol I/L urine), moderate (0.16–0.40 μmol I/L urine), or severe (<0.16 μmol I/L urine) based on criteria for establishing the severity of iodine deficiency as a public health problem (26). The categorization at the end of the study was based on mean urinary iodine excretion 5 and 11 mo after supplementation. Subsequently, children were allocated to 1 of 2 groups, the criterion for allocation being whether or not their iodine status had improved. Urinary iodine concentrations increased considerably in about two-thirds of the children (ie, status changed from severe to moderate, from

severe to normal-mild, or from moderate to normal-mild)—the “improved” group. The second, or “unchanged,” group consisted of children whose urinary iodine concentrations remained unchanged [ie, status remained moderate or normal-mild or, in a few cases ($n = 7$), from normal-mild to moderate]. None of the children in this group were severely deficient at the beginning or at the end of the study. Note that the unchanged group had, on average, better initial and end-of-study iodine status than did the improved group (Table 5). Both groups consisted of supplemented and nonsupplemented children, but proportions were not significantly different (chi-square test). Although the improved group was older than the unchanged group by 7 mo, both groups had comparable blood hemoglobin concentrations, anthropometric and socioeconomic indexes, and initial scores on the mental tests. No correlation was observed between age and change in mental performance in either of the intervention groups or in the study population as a whole (data not shown).

The performance at baseline and at the end of the study, as well as the changes in performance on the series of mental tests during the study period, were expressed as *z* scores. Thus, the *z* scores of the improved and unchanged groups together were zero, both at baseline and at the end of the study. The mean initial *z* score of the unchanged group ($n = 68$) was -0.02 ± 0.58 ,

TABLE 3
Correlation between mental development tests in the total group at the beginning of the study¹

	Spearman							
	1	2	3	4	5	6	7	8
Block design	1.00							
Closure	0.34 ²	1.00						
Concentration	0.51 ²	0.34 ²	1.00					
Exclusion	0.33 ²	0.35 ²	0.37 ²	1.00				
Fluency	0.23 ²	0.24 ²	0.39 ²	0.33 ²	1.00			
Mazes	0.44 ²	0.35 ²	0.47 ²	0.31 ²	0.29 ²	1.00		
Hand movements	0.09	-0.03	0.22 ³	0.14 ⁴	0.19 ³	0.24 ²	1.00	
Colored progressive matrixes	0.05	0.08	0.18 ⁴	-0.01	0.14 ⁴	0.06	0.16 ⁴	1.00

¹ $n = 196$.

² $P < 0.001$.

³ $P < 0.01$.

⁴ $P < 0.05$.

TABLE 4
VARIMAX-rotated factor matrix of results on mental tests at the beginning of the intervention

	VARIMAX-rotated loadings ¹			Communality
	Factor 1	Factor 2	Factor 3	
Block design	0.76			0.58
Closure	0.65			0.64
Concentration	0.73			0.60
Exclusion	0.67			0.46
Fluency	0.50			0.42
Mazes	0.65			0.49
Hand movements		0.87		0.78
Colored progressive matrixes			0.96	0.94
Sum of squares (Eigenvalue)	2.84	1.12	0.96	4.92

¹Only loadings ≥ 0.50 are included.

whereas that of the improved group ($n = 128$) was 0.01 ± 0.58 . Mean z scores at the end of the study were -0.10 ± 0.59 in the unchanged group and 0.05 ± 0.57 in the improved group. The z scores for the change in performance (ie, the differences between scores on each test at baseline and at the end of the study period) in the unchanged group were set at 0 with an SD at 1. Thus, the scores of the improved group represent the difference from the unchanged group (Table 6). Comparison of the performance on the range of tests shows a consistent pattern in favor of the improved group and the overall results in the improved group were significantly better than those in the unchanged group. With respect to the reaction-time and tapping tests, no effect of change in iodine status was shown.

DISCUSSION

This study showed that improvements in urinary iodine status in the study population reflected significantly improved mental performance on a combination of tests. Children whose urinary iodine concentrations were basically unchanged during the intervention period showed less progress in performance, even though their iodine statuses as measured by several variables were, on average, better than those of their improved counterparts both initially and at the end of the study. These findings indicate “catch-up,” ie, improvement toward full potential as a result of iodine supplementation.

The improvements in test performance found in the present study were most pronounced on the exclusion test and the colored progressive matrixes, suggesting an improvement in general abstract reasoning. Improvement was also seen on the test for verbal fluency, in agreement with the results of a study in Malawi in which improved verbal fluency was one of the most pronounced effects of iodine supplementation (9). Because all the tests used, except the colored progressive matrixes, have a time limit within which a response must be given, these findings may indicate improvement in the level of task performance, improvement in speed of task performance, or both.

Improved attention or concentration may facilitate improvement in mental function (21). According to Tiwari et al (27), iodine-deficient children are slow learners with a concurrent low “motivation to achieve.” These authors ascribe poor performance to neurologic impairment and to a paucity of psychological stimulation. In hypothyroidism, mood disorders—including depression, social withdrawal, and paucity of speech—are common phenomena (28). Thus, it may be that poor performance under conditions such as those of our study reflects a general state of apathy, accounting not only for a lack of motivation but also for other factors important in cognitive functioning, such as attentiveness and concentration.

The marked improvement in mental and psychomotor performance as a result of iodine supplementation, which was seen in a study of schoolchildren in Malawi [>10 intelligence quotient (IQ) points (9)], was not achieved in the present study. Although the iodine status of most of the children in the present study had improved substantially by the end of the intervention period, the improvement in mental performance was only ≈ 5 IQ points. The Beninese children were older than the children in Malawi (mean age: 7.1 y), but otherwise comparable in terms of initial iodine and iron statuses and in anthropometric indexes. The improvement in iodine status, whether through iodized oil supplementation or through consumption of iodized salt, may have come too late in the life of the Beninese children to enable comparable catch-up to take place.

The functional classification of children with respect to degrees of iodine deficiency remains problematic for several reasons. First, there is as yet no universally accepted single indicator for iodine status in this age group and, second, cutoff points

TABLE 5

Indicators of iodine status at the beginning and end of the intervention in groups categorized as improved or unchanged on the basis of their urinary iodine concentrations¹

	Improved group ($n = 128$)		Unchanged group ($n = 68$)	
	Initial	Final	Initial	Final
Urinary iodine concentration ($\mu\text{mol/L}$)	0.09 (0.03, 0.16) ²	0.68 (0.30, 1.25) ³	0.62 (0.40, 1.43)	0.67 (0.27, 1.28)
Serum thyroglobulin concentration (pmol/L)	285.0 (180.0, 460.0) ²	95.0 (70.5, 142.5) ³	135.0 (85.0, 225.0)	90.0 (64.0, 143.8) ³
Serum TSH concentration (mU/L) ⁴	2.20 (1.70, 3.75) ²	1.40 (1.10, 2.08) ³	1.80 (1.30, 2.45)	1.20 (1.03, 1.80) ³
Blood TSH concentration (mU/L)	4.65 (2.70, 7.80)	NA	3.75 (2.30, 6.88)	NA
Serum free T ₄ concentration (pmol/L)	11.6 \pm 2.4 ²	13.9 \pm 2.5 ^{3,5}	12.6 \pm 2.2	14.8 \pm 1.8 ³
Blood hemoglobin concentration (g/L)	115.0 \pm 1.2	118.5 \pm 1.0 ³	113.9 \pm 1.3	117.0 \pm 1.0 ³
Serum ferritin concentration ($\mu\text{g/L}$)	47.2 (30.3, 72.4)	50.9 (26.8, 104.8)	48.2 (22.3, 70.4)	48.1 (22.8, 90.4)

¹ $\bar{x} \pm \text{SD}$; 25th and 75th percentiles in parentheses. TSH, thyroid-stimulating hormone; T₄, thyroxine.

²Significantly different from initial values in unchanged group, $P < 0.05$ (independent-samples t test; nonnormally distributed variables were log transformed).

³Significantly different from initial values within the same group, $P < 0.05$ (paired-samples t test; nonnormally distributed variables were log transformed).

⁴The initial serum concentration of TSH was measured in only 154 subjects (97 in the improved group and 57 in the unchanged group).

⁵Significantly different from final values in the unchanged group, $P < 0.05$ (independent-samples t test; nonnormally distributed variables were log transformed).



TABLE 6

Change in mental performance during intervention in the group of children with improved urinary iodine concentrations¹

	<i>z</i> Score
Block design	0.05 ± 1.03 ²
Closure	0.04 ± 1.09 ²
Concentration	0.06 ± 0.87 ²
Exclusion	0.25 ± 1.00 ²
Fluency	0.18 ± 1.21 ²
Mazes	0.11 ± 0.88 ²
Hand movements	0.05 ± 1.29 ²
Colored progressive matrixes	0.24 ± 1.14
$\bar{x} \pm SE$	0.12 ± 0.06 ²


¹The mean performance for each test in the group of children with unchanged urinary iodine concentrations was set at 0 ± 1 ($\bar{x} \pm SD$).

² $\bar{x} \pm SD$.

³Significantly different from the unchanged group, $P = 0.044$ (two-tailed independent-samples *t* test).

enabling different degrees of iodine deficiency to be distinguished are based on populations rather than on individuals. The 4 iodine-status variables that we measured could not be captured in 1 variable by factor analysis, which was explained by the fact that each of these variables reflects different facets of iodine metabolism. Although initial urinary iodine concentrations indicated serious iodine deficiency in our study population, initial serum TSH and free T₄ concentrations in our group were found to be within the normal range (Table 5). These findings concur with those of Benmiloud et al (29), Pardede et al (30), and Untoro (31), who also found values for TSH and free T₄ in the normal range in studies of iodine-deficient populations. These authors, therefore, maintain that urinary iodine excretion is the best outcome indicator for interventions involving iodine supplementation. Although TSH and free T₄ concentrations improved significantly during our study, it might be argued that the normal range of TSH and free T₄ values is too wide, at least for this age group. Although the thyroglobulin concentration is considered to be very sensitive to changes in iodine metabolism, assay methods for thyroglobulin are not standardized among laboratories and, therefore, normal ranges and cutoff points for various degrees of iodine status cannot be established. For these reasons, our subjects were categorized on the basis of their urinary iodine concentrations. Although regarded as the best indicator of iodine status at the population level, the urinary iodine concentration also has its limitations, especially when used at the individual level. This is because it primarily reflects the previous day's iodine intake, which may not represent long-term intake. In addition, urinary iodine concentrations vary throughout the day. Thus, caution should be exercised in the interpretation of results.

Because of the current considerable rate of progress in universal salt iodization, further research in this field is increasingly difficult to carry out. However, constraints in iodine supply and metabolism, both in individuals and in population groups with insufficient access to sources of iodine, will continue to call for better insight into the relations between iodine status and mental functioning. Although our study showed that restoration of impaired psychoneurologic processes is to some extent still possible in schoolchildren, many questions remain. Is there an age threshold beyond which restoration is no longer possible? Are different aspects of cognitive functioning restored at different

speeds? Which iodine variables are most closely associated with changes in cognitive functioning? This study was not designed to answer these questions. However, it does indicate that mental performance of iodine-deficient children is positively influenced by iodine supplementation, whether through the use of iodized salt or the administration of iodized oil. 

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