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## **Improved iodine status is associated with improved mental performance of schoolchildren in Benin**

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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 whether iodine supplementation later in life can exert a favorable influence on mental performance of iodine deficient populations has been addressed in various studies, but with contradictory results.

**Objective:** The aim of the study was to examine the effect of an improvement of iodine status on mental and psychomotor performance of schoolchildren (7-11 yr), 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 school children (n=196) in northern Benin. As the population began to have access to iodized salt during the intervention period of 1 year, the study population was split, *post-hoc*, into a group with improved iodine status, based on increased urinary iodine concentration, 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 concentration demonstrated a significantly greater increase in performance on the combination of mental tests than did the group where the concentration did not change.

**Conclusions:** Improvement in iodine status, rather than the 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.

## **INTRODUCTION**

The public health importance of an adequate iodine supply for the physical and mental wellbeing of humankind has been well described (1,2). Most studies on the relationship 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 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 children who are growing up while iodine deficient may still benefit from iodine supplementation. In a double blind, placebo-controlled study to examine the effect of iodine supplementation of children (5.5-12 yr) on mental performance, Bautista et al (8) found no difference between supplemented and non-supplemented children. In an unpublished double-blind placebo-controlled intervention study in Malawi, iodine supplementation significantly improved performance of 6-8 year old children on a number of 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 dosing with iodized oil in school children in an iodine deficient area in northern Benin, West Africa. However, much earlier than expected, iodized salt was introduced into the study area. Halfway through the intervention period, the population began to have access to iodized salt. As iodine had become available to both groups, the hypothesis that iodine supplementation improves mental performance could no longer be tested. Therefore, we decided to test whether children whose iodine status improved over the intervention period showed a greater improvement in mental and psychomotor performance than those 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 in schoolchildren aged 6-12 yr varied from 20 to 60 % (Doh, A. and Ategbo, EA. *Prévalence de la carence en iode dans l'Atakora*; unpublished report, 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 four study villages had neither electricity nor clean drinking water.

Children from standards (grades) 2 and 3, aged 7-11 years, in the four primary schools in the study area were considered for enrolment. Since in two out of four schools all female children had been given an iodized oil supplement in the previous year, only boys were selected from these two schools.

The study was approved by the health and education authorities of the province of Atacora, and by the Medical Ethics Committee of the Division of Human Nutrition and

Epidemiology of Wageningen University. The aim of the study was explained to local administrative and traditional authorities, parents and teachers. Having obtained verbal approval from local authorities, the parents and the parents-teachers 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 matched on the basis of similar age and height-for-age. From each pair of children, one child was randomly allocated to one of two groups. The groups were then randomly allocated to receive iodine supplementation or a placebo. The study was double-blind, randomized and placebo controlled with the codes only being broken after the completion of the final test. Iodized oil (Lipiodol UF 7; 540 mg I/mL) and the placebo (poppyseed oil) were provided by Guerbet laboratories (Aulnay-sous-Bois, France). Iodized oil and poppyseed oil were dispensed as a single dose (1.0 mL), administered orally with a Swift 7 dispenser (English Glass Company, Leicester, England) in January 1996.

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

### **Somatic and biochemical indicators**

Anthropometric measurements were made in duplicate. Height was measured to the nearest mm, using a microtoise (Stanley ®). Weight was measured to the nearest 0.25 kg using a spring scale. Venous blood was drawn from the antecubical vein, immediately followed by the application of one drop of whole blood onto a filter paper card (Schleicher & Schuell, grade 903). These cards were air-dried for 1 to 2 h and packed in polyethylene bags, before being frozen. Hemoglobin was assessed using a Hemocue (Helsingborg, Sweden). Serum samples were prepared and frozen before being transported. Samples of casual urine (ca. 25 mL) were collected, to which some crystals of thymol were added. 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 Sandell-Kolthoff reaction (10); thyroid stimulating hormone (TSH) in blood spots (Spectra Screen™ Dried Blood TSH EIA Kit) and serum ferritin (ELISA), within the next 6 to 9 mo. Frozen serum samples were also transported to the Laboratory for Endocrinology, Amsterdam Medical Centre, the Netherlands for assessment of thyroglobulin (RIA), free thyroxine (time-resolved fluoroimmunoassay; Delfia™, Wallac Oy, Turku, Finland) and thyroid stimulating hormone (immunoluminometric assay; Brahms Diagnostica GmbH, Berlin, Germany).

### **Mental and psychomotor development tests**

Since no comprehensive battery of mental tests has been developed for use in French-speaking West-Africa, a number of tests, consisting of nonverbal and abstract pictorial material of the French Kaufman ABC test battery (11) was pretested in a nearby

village. Apart from the sequential memory test (hand movements), most tests contained images unknown to the children. Subsequently a battery was composed with mostly non-verbal tests which have been used under conditions comparable to those found in rural Benin, i.e. tests requiring very 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 comprised the following 8 tests: block design (15), coloured progressive matrices (16), hand movements (11) as well as 5 tests from the African Child Intelligence Test (17): closure, mazes, exclusion, concentration, and fluency. Table 1 gives a description of the tests as well as their meaning, according to factors reported by Thurstone (18) and French (19). In addition 2 psychomotor tests, pegboard and ball throwing, were carried out. A psychologist (NB) trained two university graduates and two teachers from Benin to conduct the tests, which were subsequently pretested among school children from the study area who were not included in the study population. The testers worked in pairs. All four testers started with the same three tests in a fixed sequence. The remaining tests were administered either by one tester or the other, with the same tester always being responsible for the same set of tests. All children were given a snack prior to testing, which took place between 09.00 and 12.00 hrs. in a room which was quiet and free of distractions. The 8 mental tests plus the pegboard test took approximately 50-60 mins, after which the children were taken outside for the ball throwing test. Because of the diversity and short duration of 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, based on the magnitude of change over the intervention period in urinary iodine concentration. Differences in change in mental performance between these groups were assessed using Student's t-test. If not normally distributed, log transformations were made. Factor analysis, based on the intercorrelation of the tests, was carried out, using a principal component analysis with orthogonal Varimax rotation. This enabled us to examine the construct validity of the test battery. All data were processed and analysed using SPSS-pc software (SPSS-Windows 6.1). Anthropometric indices were calculated using Epi-Info (version 6.02; CDC, Atlanta, GA, USA)

**Table 1.** Mental development tests used in the study

Test name	Test Description	Mental ability involved
Block design (WPPSI)	With a set of colored blocks (two colors; blocks having one 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 same design within a specified time period	Space <sup>1)</sup> Spatial Orientation <sup>2)</sup> Memory (partly)
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 <sup>1)</sup> Speed of closure <sup>2)</sup>
Concentration	A set of 2 pages is covered with small circles with an oblong dark "eye" in one of eight positions. The child is shown one example and is then asked to find and tick circles with the eye in the same position as the example as quickly as possible, working line by line, within a specified time period.	Perception <sup>1)</sup> Perceptual speed <sup>2)</sup>
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 one figure which lacks a common characteristic of the other three	Reasoning <sup>1)</sup> Induction <sup>2)</sup>
Fluency	In 2 fixed time periods the child is asked to mention first names of as many people as possible and subsequently, the names of as many animals as possible	Word fluency <sup>1) 2)</sup>
Mazes	The child is presented with a series of mazes en 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 <sup>1)</sup> Spatial scanning <sup>2)</sup>
Coloured Progressive Matrices (sets A, Ab, B)	The child is presented with series of coloured 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 colours 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, in order to make it complete again.	General ability Reasoning by analogy
Hand Movements (Kaufman ABC)	The child is asked to imitate series of hand movements made by the instructor on a table; movements are specified and composed of three basic elements in varying sequence and number: the fist, the side of the hand and the palm of the hand	Sequential memory

<sup>1)</sup> Based on factors according to Thurstone

<sup>2)</sup> Based on factors according to French

## RESULTS

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

### Nutritional status

One-third of the children were stunted (height-for-age  $<-2$  SD of NCHS reference), 17 % had low weight-for-age ( $<-2$  SD of NCHS reference) and 2 % were wasted (weight-for-height  $<-2$  SD of NCHS reference) (Table 2). The proportion of children with anemia (hemoglobin  $<110$  g/L) was one-third, while 11% had moderately to severely depleted iron stores (serum ferritin concentration  $< 18$   $\mu\text{g/L}$ ). With an initial median urinary iodine concentration of 0.16  $\mu\text{mol/L}$  (20.6  $\mu\text{g/L}$ ), the study population could be classified as moderately to severely iodine deficient. At the end of the intervention period both the original placebo and the iodine-supplemented group showed clearly improved iodine status. However, the total study population could still be classified as mildly iodine deficient based on median concentrations of urinary iodine. Initial urinary iodine concentration was positively correlated (Spearman) with the serum concentration of free thyroxin ( $r = 0.19$ ;  $P=0.007$ ) and negatively correlated with serum concentrations of thyroglobulin ( $r = -0.51$ ;  $P=0.000$ ) and thyroid stimulating hormone ( $r = -0.34$ ;  $P=0.000$ ). At the end of the study urinary iodine concentration was related with serum thyroglobulin concentration only ( $r = -0.21$ ;  $P=0.003$ ).

**Table 2.** General characteristics of subjects and their families <sup>1)</sup>

Characteristics of subjects	Improved group		Unchanged group	
	Initial	Final	Initial	Final
n (males/females)		128 (109/19)		68 (58/10)
Suppl./non-suppl.		68/60		29/39
Age (y)	9.1 $\pm$ 1.2	10.1 $\pm$ 1.2	8.5 $\pm$ 1.2	9.5 $\pm$ 1.2
Height-for-age (Z-score)	-1.73 $\pm$ 0.91	-1.70 $\pm$ 0.87	-1.48 $\pm$ 1.04	-1.43 $\pm$ 1.01
Weight-for-age (Z-score)	-1.35 $\pm$ 0.70	-1.38 $\pm$ 0.70	-1.32 $\pm$ 0.77	-1.33 $\pm$ 0.75
Education (y)	2.8 $\pm$ 0.9		2.6 $\pm$ 0.7	
<i>Characteristics of family</i>				
Family size (n)	14.2 $\pm$ 7.2		14.8 $\pm$ 8.4	
Education of parents (y)				
- father	1.3 $\pm$ 0.8		1.4 $\pm$ 0.9	
- mother	1.2 $\pm$ 0.5		1.3 $\pm$ 0.8	
Size of landholding (ha)	3.1 $\pm$ 2.4		3.2 $\pm$ 2.7	

<sup>1)</sup> Results are expressed as mean  $\pm$  SD, except for the number and proportion of supplemented/non-supplemented subjects



### Mental performance

Correlations between the scores on the different tests at baseline were mostly positive (Table 3), in line with what is usually found (20). Factor analysis of the series of tests used followed by Varimax rotation produced three factors. Block design, closure, exclusion, maze, fluency and concentration tests loaded on one factor, the hand movements test on the second factor and the Coloured Progressive Matrices or Raven test loaded on the third factor (Table 4). This pattern is similar to the pattern found in a study on an intelligence test for Dutch, Spanish and Indian children, and comparison of this battery with the WISC-R battery (21-23). The first factor refers to spatial/perceptual reasoning skills, the second factor to sequential memory and the third factor to general intelligence, often referred to as *g* (20,24). The overall changes in performance over the intervention period were small but positive. Test-retest correlation of the full test battery in the unchanged group was 0.83 ( $P=0.000$ ).

**Table 3.** Correlation between mental development tests in total group ( $n=196$ ), at the beginning of the study

	<i>Spearman correlation coefficients</i>							
	1	2	3	4	5	6	7	8
1. Block design	1.00							
2. Closure	0.34***	1.00						
3. Concentration	0.51***	0.34***	1.00					
4. Exclusion	0.33***	0.35***	0.37***	1.00				
5. Fluency	0.23***	0.24***	0.39***	0.33***	1.00			
6. Mazes	0.44***	0.35***	0.47***	0.31***	0.29***	1.00		
7. Hand movements	0.09	-0.03	0.22**	0.14*	0.19**	0.24***	1.00	
8. Raven test	0.05	0.08	0.18*	-0.01	0.14*	0.06	0.16*	1.00

Significance of correlation coefficients: \*  $P<0.05$ ; \*\*  $P<0.01$ ; \*\*\*  $P<0.001$

**Table 4.** Varimax-rotated factor matrix of results on mental tests at the beginning of the study

	VARIMAX-rotated Loadings <sup>1)</sup>			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
Raven test			0.96	0.94
				Total
Sum of squares (Eigenvalue)	2.84	1.12	0.96	4.92

<sup>1)</sup> Only loadings  $\geq 0.50$  are included

### Mental performance in relation to iodine status

Children were categorized (Table 5) both at the beginning and the end of the study with respect to their urinary iodine concentration as *normal/mild* ( $>0.40 \mu\text{mol I/L}$  urine), *moderate* ( $0.16 - 0.40 \mu\text{mol I/L}$  urine) or *severe* ( $<0.16 \mu\text{mol I/L}$  urine) based on criteria for establishing the severity of iodine deficiency as a public health problem (25). The categorization at the end of the study was based on the mean urinary iodine excretions at 5 months and 11 months after supplementation. Subsequently children were allocated to one of two groups, the criterion for allocation being whether or not they moved to a better category of iodine status. About two-thirds of the children, forming the “improved” group, showed a considerable increase in urinary iodine concentration (i.e. their status had moved from the severe to the moderate or mild/normal categories or, alternatively, from the moderate to the mild/normal category). The second or “unchanged” group comprised children whose urinary iodine concentration remained unchanged (i.e. they remained in the moderate or mild/normal categories or, in a few cases ( $n=7$ ), they changed from mild/normal to moderate deficiency. None of the children in this group were severely deficient either at the beginning or at the end of the study). It should be noted that the unchanged group had, on average, better initial and end-of-study iodine status than their counterparts in the improved group (Table 5). Both groups comprised supplemented and non-supplemented children, but frequencies were not significantly different (Chi-Square test). Although the improved group was older than the unchanged group by 7 mo, groups were fully comparable in terms of blood hemoglobin concentrations, anthropometric and socio-economic indices as well as initial scores on the mental tests. No correlation was observed between age and change in mental performance in either one of the intervention groups or in the study population as a whole (data not shown).

**Table 5.** Indicators of iodine status <sup>1)</sup> at beginning and end of the intervention in groups categorized as improved or unchanged on the basis of urinary iodine concentration (n=196)

	Improved		Unchanged	
	Initial	Final	Initial	Final
Urinary iodine concentration ( $\mu\text{mol/L}$ )	0.09 (0.03; 0.16) <sup>4,5)</sup>	0.68 (0.30; 1.25)	0.62 (0.40; 1.43)	0.67 (0.27; 1.28)
Serum thyroglobulin concentration (pmol/L)	285.0(180.0; 460.0) <sup>4,5)</sup>	95.0 (70.5; 142.5)	135.0 (85.0; 225.0) <sup>4)</sup>	90.0 (64.0; 143.8)
Serum TSH concentration (mU/L) <sup>2)</sup>	2.20 (1.70; 3.75) <sup>4,5)</sup>	1.40 (1.10; 2.08)	1.80 (1.30; 2.45) <sup>4)</sup>	1.20 (1.03; 1.80)
Blood TSH concentration (mU/L)	4.65 (2.70; 7.80)	n.a. <sup>3)</sup>	3.75 (2.30; 6.88)	n.a. <sup>3)</sup>
Serum free T4 concentration (pmol/L)	11.6 $\pm$ 2.4 <sup>4,5)</sup>	13.9 $\pm$ 2.5 <sup>6)</sup>	12.6 $\pm$ 2.2 <sup>4)</sup>	14.8 $\pm$ 1.8
Blood hemoglobin concentration (g/L)	115.0 $\pm$ 1.2 <sup>4)</sup>	118.5 $\pm$ 1.0	113.9 $\pm$ 1.3 <sup>4)</sup>	117.0 $\pm$ 1.0
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)

<sup>1)</sup> Values are expressed as means  $\pm$  SD or as median (25th; 75th percentile)

<sup>2)</sup> The initial serum concentration of TSH was measured in only 154 subjects (97 in the improved group, 57 in the unchanged group)

<sup>3)</sup> Not available

<sup>4)</sup> Initial/final values within same group are significantly different ( $P < 0.05$ ); paired samples t-test (non-normally distributed variables were log transformed)

<sup>5)</sup> Initial values between groups are significantly different ( $P < 0.05$ ); independent samples t-test (non-normally distributed variables were log transformed)

<sup>6)</sup> Final values between groups are significantly different ( $P < 0.05$ ); independent samples t-test (non-normally distributed variables were log transformed)

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  $-0.02 \pm 0.58$ , while that of the improved group (n=128) was  $0.01 \pm 0.58$ . Mean Z-scores at the end of the study were  $-0.10 \pm 0.59$  in the unchanged group and  $0.05 \pm 0.57$  in the improved group. The Z-scores for the change in performance (i.e. 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. Comparison of the performance on the range of tests shows a consistent pattern in favor of the improved group (Table 6) 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 could be demonstrated.

**Table 6.** Change in mental performance during intervention in the group of children with improved urinary iodine concentration <sup>1)</sup>

	Z-scores
Block design	$0.05 \pm 1.03$
Closure	$0.04 \pm 1.09$
Concentration	$0.06 \pm 0.87$
Exclusion	$0.25 \pm 1.00$
Fluency	$0.18 \pm 1.21$
Mazes	$0.11 \pm 0.88$
Hand movements	$0.05 \pm 1.29$
Colored progressive matrices (Raven test)	$0.24 \pm 1.14$
Mean $\pm$ SE	$0.12 \pm 0.06$ <sup>2)</sup>

<sup>1)</sup> Z-scores, mean  $\pm$  SD. Mean performance for each test in the group of children with unchanged urinary iodine concentration was set at  $0 \pm 1$  (mean  $\pm$  SD)

<sup>2)</sup> Significantly different from unchanged group ( $P=0.044$ ; 2-tailed independent samples t-test)

## DISCUSSION

This study demonstrates that in this population improvement of urinary iodine concentration is reflected in significantly improved mental performance on a combination of tests. Children whose urinary iodine concentration was basically unchanged during the intervention period showed less progress in performance, even though their iodine status as measured by several variables was, on average, better than that of their improved counterparts both initially and at the end of the study. These findings are indicative of "catch-up", that is, improvement towards their full potential, as a result of iodine supplementation.

The improvement found in the present study is most pronounced in tests on exclusion and the coloured progressive matrices or Raven test, suggesting an improvement

in general abstract reasoning. Improvement was also seen on the test for verbal fluency. The latter finding concurs with a study in Malawi in which improved verbal fluency was one of the most pronounced effects of iodine supplementation (9). Since all tests, except for the coloured progressive matrices, have a time limit within which a response must be given, these findings may point to improvement in the level of task performance, improvement in speed of task performance, or a combination of the two.

Improved attention or concentration may facilitate improvement in mental function (20). According to Tiwari and colleagues (26) iodine deficient children are slow learners with a concurrent low "motivation to achieve". They ascribe poor performance to both neurologic impairment and paucity of psychologic stimulation. In hypothyroidism, mood disorders including depression, social withdrawal, and paucity of speech are common phenomena (27). Thus it may well be that poor performance under conditions as found in our study reflects a general state of apathy, accounting not only for the 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 in schoolchildren in Malawi (>10 IQ points; (9)), was not achieved in the present study. Although by the end of the intervention period the iodine status of the majority of children had improved substantially, the improvement in mental performance amounted to approximately 5 IQ points. The Beninese children were older than the children in Malawi (mean age 7.1 yr), but otherwise comparable in terms of initial iodine and iron status and in anthropometric indices. The improvement in iodine status, whether through iodized oil supplementation or through iodized salt, may have come too late in their life 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. Firstly, there is as yet no universally accepted single indicator for "iodine status" in this age group and secondly, cut-off points enabling different degrees of iodine deficiency to be distinguished are based on populations rather than on individuals. The four iodine status variables which we measured could not be captured in one variable by factor analysis, which can be explained by the fact that each of these variables reflects different facets of iodine metabolism. While initial urinary iodine concentrations were indicative of a 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 (28), Pardede et al (29) and Untoro et al (30) who, in studies in iodine deficient populations, also find values for TSH and free T4 in the normal range. These authors therefore maintain that urinary iodine excretion is the best outcome indicator for interventions involving iodine supplementation. As in our study TSH and free T4 concentrations showed significant improvement over the study period, it might also be argued that the normal range of TSH and free T4 values is too wide, at least for this age group. Although 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 cut-off 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 alternative for measuring iodine status at the population level, using 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 be representative of long term intake. In addition, urinary iodine concentrations vary throughout the day. Thus, caution should be exercised in the interpretation of results.

With the current rate of progress being made with 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 a better insight into the relationships between iodine status and mental functioning. While our study has shown that restoration of impaired psycho-neurological processes is to some extent still possible in school children, a number of 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 set up to answer these questions. It does however 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.

#### References

1. Bleichrodt N, Born MP. A metaanalysis of research on iodine and its relationship to cognitive development. In: Stanbury JB, ed. *The damaged brain of iodine deficiency*. New York: Cognizant Communication Corporation, 1994:195-200.
2. Hetzel BS, Pandav C, Eds. *SOS for a billion- the conquest of iodine deficiency disorders*. Oxford: Oxford University Press, 1994.
3. Pharoah POD, Connolly KJ. Effects of maternal iodine supplementation during pregnancy. *Arch Dis Child* 1991;145-147.
4. Fierro-Benitez R, Cazar R, Stanbury J, Rodriguez F, Fierro-Renoy F. Effects on schoolchildren of prophylaxis of mothers with iodized oil in an area of iodine deficiency. *J Endocrinol Invest* 1988;11:327-335.
5. Pharoah POD, Connolly KJ, Ekins R, Harding A. Maternal thyroid hormone levels in pregnancy and the subsequent cognitive and motor performance of the children. *Clin Endocrinol* 1984;21:265-270.
6. Cao XY, Jiang XM, Dou ZH, et al. Timing of vulnerability of the brain to iodine deficiency in endemic cretinism. *N Engl J Med* 1994;331:1739-1744.
7. DeLong GR. Iodine and brain development. *Dev Med Child Neurol* 1996;38:279-280.
8. Bautista A, Barker PA, Dunn JT, Sanchez M, Kaiser DL. The effects of oral iodized oil on intelligence, thyroid status, and somatic growth in school-age children from an area of endemic goiter. *Am J Clin Nutr* 1982;35:127-134.
9. Shrestha RM. *Effect of iodine and iron supplementation on physical, psychomotor and mental development in primary school children in Malawi*. Wageningen: Thesis; Wageningen Agricultural University, 1994.
10. Dunn J, Crutchfield H, Gutekunst R, Dunn A. *Methods of measuring iodine in urine*. Wageningen: ICCIDD/UNICEF/WHO, 1993.
11. Kaufman A, Kaufman N. *K-ABC; Batterie pour l'examen psychologique de l' enfant*. ECPA; Les Editions du Centre de Psychologie Appliquee, 1993.
12. Cattell R. Theory of fluid and crystallized intelligence: A critical experiment. *J Educ Psychol* 1963;54:1-22.
13. Cattell R. *La théorie d'intelligence fluide et cristallisé, sa relation avec les tests 'culture fair' et sa vérifications chez les enfants de 9 a 12 ans*. (The theory of fluid and crystallized

- intelligence, its relation with 'culture fair' tests and its verification with children of 9 to 12 years). *Rev Psychol Appl* 1967;17:134-154.
14. Cattell R. The theory of fluid and crystallized general intelligence checked at the 5-6 year-old level. *Br J Educ Psychol* 1967;37:209-244.
  15. Wechsler D. Wechsler preschool and primary scale of intelligence, WPPSI. San Antonio: The Psychological Corporation, 1967.
  16. Raven J. Coloured progressive matrices. 10th ed. Oxford: Oxford Psychologists Press Ltd, 1993.
  17. Drenth P, Van der Vlier H, Muinde N, Otaala B, Omari I, Opolot J. African child intelligence test/Jaribio akili mtoto Afrika. Free University of Amsterdam, University of Nairobi, University of Dar es Salaam, 1980.
  18. Thurstone LL. Primary mental abilities. *Psychometric Monographs* 1938;1:
  19. Ekstrom RB, French JW, Harman HH. Cognitive factors: their identification and replication. *Multivariate Behavioral Research Monographs* 1979;2:1-34.
  20. Carroll J. Human cognitive abilities; a survey of factor-analytic studies. 1st ed. Cambridge: Cambridge University Press, 1993.
  21. Bleichrodt N, Resing W, Drenth P, Zaal J. Intelligentie-meting bij kinderen (Measuring intelligence in children). Lisse: Swets & Zeitlinger B.V., 1987.
  22. Bleichrodt N, Escobar del Rey F, Morreale de Escobar G, Garcia I, Rubio C. Iodine deficiency, implications for mental and psychomotor development in children. In: Delong GR, Robbins J, Condliffe PG, eds. *Iodine and the brain*. New York: Plenum Press, 1989:269-288.
  23. Bleichrodt N, Hoksbergen R, Khire U. Cross-cultural testing of intelligence. *Cross-Cult Res* 1999;33:3-25.
  24. Cronbach L. *Essentials of psychological testing*. 5th ed. New York: HarperCollins, 1990.
  25. WHO, UNICEF, ICCIDD. Indicators for assessing iodine deficiency disorders and their control through salt iodization. Geneva: WHO, 1994.
  26. Tiwari BD, Godbole MM, Chattopadhyay N, Mandal A, Mithal A. Learning disabilities and poor motivation to achieve due to prolonged iodine deficiency. *Am J Clin Nutr* 1996;63:782-786.
  27. Esposito S, Prange AJJ, Golden RN. The thyroid axis and mood disorders: overview and future prospects. *Psychopharmacol Bull* 1997;33:205-217.
  28. Benmiloud M, Chaouki ML, Gutekunst R, Teichert HM, Wood WG, Dunn JT. Oral iodized oil for correcting iodine deficiency: Optimal dosing and outcome indicator selection. *J Clin Endocr Metab* 1994;79:20-24.
  29. Pardede LV, Hardjowasito W, Gross R, et al. Urinary iodine excretion is the most appropriate outcome indicator for iodine deficiency at field conditions at district level. *J Nutr* 1998;128:1122-1126.
  30. Untoro J, Schultink W, Gross R, West CE, Hautvast JGAJ. Efficacy of different types of iodised oil. *Lancet* 1998;351:752-753.