Iodine supplementation improves cognition in iodine-deficient schoolchildren in Albania: a randomized, controlled, double-blind study[1–4]

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ABSTRACT

Background: Iodine is required for the production of thyroid hormones, which are necessary for normal brain development and cognition. Although several randomized trials examined the effect of iodine supplementation on cognitive performance in schoolchildren, the results were equivocal.

Objective: We aimed to ascertain whether providing iodized oil to iodine-deficient children would affect their cognitive and motor performance.

Design: In a double-blind intervention trial, 10–12-y-old children ($n = 310$) in primary schools in rural southeastern Albania were randomly assigned to receive 400 mg I (as oral iodized oil) or placebo. We measured urinary iodine (UI), thyroid-stimulating hormone (TSH), and total thyroxine (TT_4) concentrations and thyroid gland volume (by ultrasound). The children were given a battery of 7 cognitive and motor tests, which included measures of information processing, working memory, visual problem solving, visual search, and fine motor skills. Thyroid ultrasound and the biochemical and psychological tests were repeated after 24 wk.

Results: At baseline, the children's median UI concentration was 43 μg/L; 87% were goitrous, and nearly one-third had low concentrations of circulating TT_4. Treatment with iodine markedly improved iodine and thyroid status: at 24 wk, median UI in the treated group was 172 μg/L, mean TT_4 was ≈40% higher, and the prevalence of hypothyroxinemia was < 1%. In the placebo group after the intervention, these variables did not differ significantly from baseline. Compared with placebo, iodine treatment significantly improved performance on 4 of 7 tests: rapid target marking, symbol search, rapid object naming, and Raven's Coloured Progressive Matrices ($P < 0.0001$).

Conclusion: Information processing, fine motor skills, and visual problem solving are improved by iodine repletion in moderately iodine-deficient schoolchildren. *Am J Clin Nutr* 2006;83: 108–14.

KEY WORDS Iodine, deficiency, Albania, children, cognition, goiter, iodized oil

INTRODUCTION

Globally, > 1.9 billion persons, including 285 million children, have an inadequate iodine intake (1). Iodine is required for the production of thyroid hormones, which are essential for normal brain development; the fetus and newborn are particularly vulnerable to iodine deficiency (2). The adverse effects of in utero iodine deficiency on neuromotor development are well established: randomized controlled trials showed that iodine supplementation in iodine-deficient mothers before pregnancy or during early pregnancy improves the motor and cognitive performance of their offspring (3–5).

The postnatal effects of iodine deficiency on cognitive function are much less clear. Observational studies of children living in iodine-deficient areas have generally found evidence of impaired intellectual function and fine motor skills as compared with those in children in iodine-sufficient areas (6–8). From a meta-analysis of these and other studies, it has been estimated that populations with chronic iodine deficiency experience a reduction of 13.5 points in intelligence quotient (9). This evidence is suggestive, but observational studies are often confounded by other environmental factors that affect child development, such as health, socioeconomic status, and the accessibility and quality of education (10). Moreover, these studies could not distinguish between the persistent effects of in utero iodine deficiency and the effects of current iodine status. Several randomized trials have examined the effect of iodine supplementation on the cognitive performance of children, but their results are equivocal, and problems of method limit their interpretation (11–17).

Thus, although schoolchildren are a main target group of iodine prophylaxis (1), the benefits of iodine repletion in this age group are unclear. The question remains as to whether, for a child

born and raised under conditions of iodine deficiency, iodine treatment is remedial. Rural areas of southern Albania are severely iodine deficient; a 2003 study reported a median urinary iodine (UI) concentration of 17 μg/L and a goiter rate of $> 75\%$ in schoolchildren (18). Our study aim was to ascertain whether providing iodized oil to iodine-deficient Albanian schoolchildren would affect their cognitive and motor function.

SUBJECTS AND METHODS

Subjects

The study was done in 7 primary schools in villages (ie, Lozhan, Proptisht, Slabinje, Golik, Katjel, Rodokal, and Homezh) in the Korçe/Pogradeç district of southeastern Albania. These rural villages each have 500–3000 inhabitants. The elevation of the villages is 400–800 m. Isolated from commercial routes, they are located in a mountainous region where electricity is intermittent, and access is generally by unpaved road. Local food staples are wheat bread, goat cheese, cabbage, and white beans. Most household salt is not iodized, and the region is severely iodine deficient (18). All 10–12-y-old children at the schools were invited to join the study.

The height and weight of the children were measured by using standard anthropometric techniques (19). For the measurements, subjects removed their shoes, emptied their pockets, and wore indoor clothing. A spot morning urine sample was collected for measurement of UI concentration. Whole blood from a finger prick was spotted onto filter-paper cards (Grade 903; Schleicher & Schuell, Einbeck, Germany) and allowed to dry at room temperature. The dried blood spots were used for measurement of whole blood thyroid-stimulating hormone (TSH) and serum total thyroxine (TT_4) concentrations. Thyroid gland volume was measured in children who were sitting upright by using a portable Aloka SSD-500 Echocamera (Aloka, Mure, Japan) with a 7.5-MHz 5-cm linear transducer. One of the investigators (MBZ) performed all ultrasound measurements by using validated techniques (20).

The psychological testing of the children was carried out in their schools. Because these rural schools have only intermittent electricity, paper and pencil procedures were used, and timing was done with battery-driven electronic stop-clocks. Tests were chosen for their simplicity and ease of administration, as well as their sensitivity to iodine deficiency or hypothyroidism (or both) in previous studies (*see* Discussion). The 7 tests employed (21–25) are described below. They took each child ≈25 min to complete.

Written informed consent was obtained from the parents of each child, and oral assent was obtained from the children. Ethical approval for the study was given by the Swiss Federal Institute of Technology Zürich and the Ministry of Health of Albania.

Methods

Raven's Coloured Progressive Matrices

Raven's Coloured Progressive Matrices have been used extensively as a "culture-fair" test of intelligence. They measure the ability to reason and solve problems. The test is made up of 3 sets of 12 visual problems. The subject is shown a visual pattern with a missing section and is required to select 1 of 6 alternative sections to complete the overall pattern (23). As the test proceeds, the problems become progressively more difficult. The test is not timed, and the subject continues until satisfied with the choice made. There are 2 equivalent forms of the test, classic and parallel, in which difficulty levels are matched overall and on an item-per-item basis. The classic form was used for baseline measures, and the parallel form was used for the 24-wk follow-up measures. The score is the number of correct items selected.

Coding

The coding test is taken from the Wechsler Intelligence Scale for Children (24). The child copies simple symbols, each of which is paired with a digit from 1 to 9. After demonstration by the tester and a brief period of practice, the child is given a sheet with 93 numbers and asked to put the appropriate symbol next to each number as quickly as possible. The score is the number of correct matches made in 120 s.

Symbol search

This visual search/matching task is taken from the Wechsler Intelligence Scale for Children, level B (24). The child is asked to scan 2 groups of symbols, a target group and a search group. If a symbol occurs in both groups, a "yes" box is to be marked; if it does not, a "no" box is to be marked. The need to work as quickly as possible is stressed. The score is the number of correct answers minus the number of incorrect answers in 120 s.

Digit span

The digit span test is a simple test of short-term memory. The scoring procedure used was that employed in the Wechsler Intelligence Scale for Children (24). The examiner reads a series of number sequences at the rate of 1/s. The child is asked to repeat the sequence in the same order. After a correct repetition, the list is increased by 1 sequence. The test ends if a child fails 2 successive number sequences at a given list length. After digit span forward, the test is repeated backwards; that is, the list must be recalled in reverse order. The score is the number of sequences correctly recalled. The test is not timed.

Rapid object naming

The rapid object-naming test is designed to measure the speed at which a child is able to name a series of familiar objects. The child is shown a card with line drawings of 20 objects. When the child has named these objects, he or she is given another card with 2 sets of objects and asked to name them as quickly as possible. The score is the time taken. An adjustment is made for errors (25).

Bead threading

The bead-threading test is a measure of fine motor skill and involves threading small, brightly colored beads onto a thin string (5). The child is asked to thread as many beads as possible in 60 s. The task is repeated 3 times, and the score is the mean number of beads threaded.

Rapid target marking

In rapid target marking, the child is given a pencil and a target sheet, fixed to a clipboard, on which targets are arranged in rows. The targets are circles 3 mm in diameter; there is an 8-mm space between centers. The task is to strike through each target as quickly as possible. Following the tester's demonstration and the child's practice, the child is given a test sheet with 3 sets of 45

btargets. The time taken to strike through a set of targets is recorded, and the mean of the 3 sets is the score.

The children were tested by a team of 10 testers composed of members of the professional staff (psychologists and pediatricians) of the Child Development Centre in Tirana, Albania, and graduates in psychology from Tirana University. All but one of the testers were female. The testers were trained for 4–5 d. Ten testers were used to complete the testing of all of the children over ≈10 d. The purpose and design of the study were explained, and the 7 tests were introduced. The testers were competent in English but were also given detailed written instructions in Albanian for each of the tests. These instructions were translated from English by a native Albanian who is fluent in English and then were checked by a second Albanian speaker. The testers watched while each of the tests was administered, and then they tested each other. The testers then tested, under supervision, 10–12-y-old children recruited for this purpose from a primary school in Tirana. Before the retesting at 24 wk, a refresher session on the tests and their administration was given. Test-retest reliability was estimated by testing 30 schoolchildren, boys and girls, on each of the tests and then testing them again 14 d later. The children were not retested by the same tester. Children used in the estimation of test reliabilities were the same age as the study population, but they were not participants in the subsequent intervention study. Correlations between the 2 scores for each test were: Raven's Coloured Progressive Matrices, 0.80; digit span, 0.78; coding, 0.74; symbol search, 0.54; rapid object naming, 0.71; bead threading, 0.52; and rapid target marking, 0.68.

After completing the baseline testing, the children were randomly assigned to receive 400 mg oral I as iodized poppyseed oil (26) (Lipiodol; Guerbet SA, Roissy CdG Cedex, France) or a sunflower oil–containing placebo. The group assignments were done by using Excel software (version XP 2002; Microsoft, Redmond, WA) with the random-number-generator function and by using a Bernoulli distribution ($P = 0.5$), in which random variables have the value 0 or 1. The capsules were swallowed with water under direct supervision. The study design was double-blind. Children were tested at baseline in September 2004 and retested in March 2005, or 23–24 wk after receiving the treatment or placebo. After the second round of testing was complete, all children in the study received 400 mg oral I (26).

Laboratory analysis

Urine samples were aliquoted and frozen at −20 °C until analysis. UI concentrations were measured by using a modification of the Sandell-Kolthoff reaction (27). At UI concentrations of 47 and 79 μg/L, the CV of this assay in our laboratory is 10.3 and 12.7%, respectively. Dried blood spots on filter paper were analyzed for whole-blood TSH and serum TT_4 by using immunoassays (28). Normal reference values are < 3.7 mU/L for TSH and 65–165 nmol/L for TT_4. Thyroid volume was calculated from ultrasound measurements, and goiter was classified according to sex- and body surface area–specific reference criteria (20). To estimate intraobserver variability, duplicate thyroid measurements were done in 20 children; the mean (±SD) variability was 3.5 ± 1.9%.

Statistical analysis

Data were analyzed by using SPLUS (version 2000; Insightful Corporation, Seattle, WA) and Excel software. Non-normally distributed data (UI, TSH, and thyroid volume) were log transformed for comparisons. A 2-factor analysis of variance was used to ascertain the interaction between time and treatment for UI, TSH, TT_4, and thyroid volume. Post hoc comparisons were done by using paired Wilcoxon's tests and McNemar's tests within groups and unpaired Wilcoxon's tests and chi-square tests between groups. Follow-up values on the cognitive and motor tests were analyzed by using mixed-models analysis of variance with school as a random effect and group, regression on the corresponding baseline value, and sex as fixed effects. Multiple regressions were done with the 7 baseline and follow-up values on the tests as the dependent variable and the corresponding TSH, TT_4, and thyroid volume values, as well as sex, school, and group, as independent variables. Baseline data from children who did not complete the biochemical or cognitive retesting (or both) were not included in the analysis. Significance was set at $P < 0.05$.

RESULTS

The study population ($n = 310$) included 166 boys and 144 girls aged 10–12 y. The mean age of the iodine ($n = 159$) and placebo ($n = 151$) groups was 11.3 ± 0.8 y and 11.5 ± 0.8 y, respectively (NS). The ratio of boys to girls was 1.2 in the iodine group and 1.1 in the placebo group. The mean weight and height of the iodine and placebo groups were 32.9 ± 5.5 kg and 139 ± 8 cm and 33.9 ± 6.6 kg and 140 ± 8 cm, respectively (NS). Six children moved away during the study and did not complete the cognitive retesting: 4 in the iodine group and 2 in the placebo group. Thyroid function tests were not measured at follow-up in 12% of the children because they refused blood sampling.

At baseline, 87% of the children were goitrous, according to thyroid volume measurements made with ultrasound (20). The concentrations of UI, TSH, and TT_4; thyroid volume; and the prevalence of hypothyroxinemia (as defined by $TT_4 < 65$ nmol/L) in the children at baseline and after intervention are shown in **Table 1**. The cognitive and motor test scores in the subjects before and after receiving either iodine or placebo are shown in **Table 2**. Despite randomization, there were significant differences between groups at baseline on Raven's Coloured Progressive Matrices ($P < 0.0001$), bead threading ($P = 0.04$), rapid target marking ($P = 0.02$), and symbol search ($P < 0.0001$). To adjust for baseline differences between groups, the test data were analyzed by using a mixed-model analysis of variance with regression on the individual baseline as a fixed effect. Iodine treatment was associated with highly significant improvement in test scores on Raven's Coloured Progressive Matrices, rapid target marking, symbol search, and rapid object naming ($P < 0.0001$). There was no significant sex × treatment group interaction. However, in both the treatment and control groups, there was a significant effect of sex: girls scored significantly better on the tests of rapid target marking (1.9; $P = 0.002$), symbol search (0.85; $P = 0.04$), and rapid object naming (2.8; $P = 0.01$) than did boys. Multiple regressions showed no significant effect of TT_4, TSH, or thyroid volume on any of the baseline or follow-up values or on the change from baseline values on the cognitive tests.

DISCUSSION

At baseline, the children were moderately to severely iodine deficient, as defined by a median UI of 44 μg/L and a goiter rate

TABLE 1
Concentrations of urinary iodine, whole-blood thyroid-stimulating hormone (TSH), and serum total thyroxine (TT$_4$); thyroid volume; and the prevalence of hypothyroxinemia in 10–12-y-old Albanian schoolchildren at baseline and 24 wk after intervention[1]

Variable and time	Iodine treatment group		Control group	
	n	Value	n	Value
Urinary iodine (μg/L)[2]				
0	157	42 (0–186)[3]	146	44 (0–215)
24 wk	154	172 (18–724)[4,5]	145	49 (3–221)
Thyroid volume (mL)[2]				
0	142	5.9 (2.6–12.5)	132	6.2 (2.1–16.8)
24 wk	148	5.0 (2.4–9.7)[6,7]	145	6.3 (2.6–16.0)
TSH (mU/L)				
0	159	0.8 (0.3–2.5)	151	0.9 (0.4–2.6)
24 wk	134	0.7 (0.2–2.6)	130	0.8 (0.2–7.7)
TT$_4$ (nmol/L)[2]				
0	159	76 ± 17[8]	151	75 ± 17
24 wk	134	106 ± 18[6,7]	130	81 ± 19
TT$_4$ < 65 nmol/L [n (%)]				
0	159	46 (29)	151	47 (31)
24 wk	134	1 (0.7)[9,10]	130	30 (23)

[1] Intervention was 400 mg I (as oral iodized oil) or placebo. Hypothyroxinemia was defined as a TT$_4$ concentration < 65 nmol/L.

[2] Significant time × treatment interaction, $P < 0.0001$ (ANOVA).

[3] Median; range in parentheses (all such values).

[4,6] Significantly different from baseline (paired Wilcoxon test): [4]$P < 0.0001$, [6]$P < 0.01$.

[5,7] Significantly different from control group (unpaired Wilcoxon test): [5]$P < 0.001$, [7]$P < 0.01$.

[8] $\bar{x} \pm$ SD (all such values).

[9] Significantly different from baseline, $P < 0.0001$ (McNemar's test)

[10] Significantly different from control group, $P < 0.0001$ (chi-square test).

of 87% (goiter measured with ultrasound) (2). Nearly one-third of the children had low circulating TT$_4$ concentrations because of chronic iodine deficiency. Treatment with iodized oil produced a marked and sustained improvement in iodine status. At follow-up, median UI in the treated group was 172 μg/L, and only 13% of the treated children had a UI < 50 μg/L. Treatment also significantly improved thyroid function: median thyroid volume fell by 18%, mean TT$_4$ increased ≈40%, and the prevalence of hypothyroxinemia was reduced to < 1%. There was no "spill-over" of the iodine in the control subjects: the baseline median UI, median thyroid volume, and mean TT$_4$ were unchanged at follow-up.

Compared with the placebo, iodine treatment significantly improved performance on 4 of the 7 tests: rapid target marking, symbol search, rapid object naming, and Raven's Coloured Progressive Matrices. A measure of the efficiency of cognitive processes is provided by the time taken to execute them (29, 30). Iodine treatment improved information processing rates, as measured by the symbol search, rapid-object-naming, and rapid-target-marking tests. Raven's Coloured Progressive Matrices measure the ability to reason and solve problems involving new information without relying on an explicit base of declarative knowledge (31). The adjusted treatment effect of 4.7 points on Raven's Coloured Progressive Matrices suggests that iodine repletion was associated with a small but significant increase in intelligence. Performance on both the forward and backward digit-span tests was unaffected by iodine treatment. Several studies exploring the effects of iodine deficiency on development found that motor skill and dexterity were significantly affected (5, 32). Although iodine treatment improved performance on the rapid-target-marking test, it did not affect the second manual test

of bead threading. Threading beads is a more complex action that requires the 2 hands to work together in a series of interlocking routines. The task can be done in a number of ways, depending on which hand is stationary and which moves—the hand holding the bead or the hand holding the lace. A child doing the task with little experience or practice typically employs a varied action plan until one strategy emerges as predominant. The variability in strategy used in the early stages probably explains the modest test-retest reliability with this test.

We tested speed of processing because it may be more sensitive than are other cognitive functions to nutritional deficits (33) and, in particular, more sensitive to hypothyroidism (34, 35). It is likely that current iodine deficiency impairs cognitive function through reduced thyroid function (36). Chronic hypothyroidism (34, 35), even when subclinical (37), has adverse effects that include slowing of intellectual function and speech, impaired attention and vigilance, and memory deficits. In older adults, serum thyroxine (T$_4$) concentrations and scores on cognitive tests are correlated, and the treatment of hypothyroidism significantly improves measures of cognition (38). In iodine-deficient children, those with lower T$_4$ concentrations have significantly poorer scores on reading and spelling tests than do those with higher T$_4$ concentrations (39). The mechanism for these effects is unclear. Short-term deficiency in thyroid hormones results in a generalized decrease in regional cerebral blood flow and brain activity (40). Intracerebral triiodothyronine (T$_3$), the active form of thyroid hormone in the brain, is generated locally from T$_4$ and is correlated with serum T$_4$ but not with serum T$_3$ (41). Thyroid hormone has several molecular targets in the brain, including genes involved in myelination and the synthesis of neurogranin, a brain-specific, calmodulin-binding, protein kinase C substrate

TABLE 2
Cognitive and motor test scores in 10–12-y-old Albanian children at baseline and 24 wk after intervention[1]

Test and time	Iodine treatment group (n = 159)	Control group (n = 151)	Mean adjusted treatment effect (95% CI)
Raven's Coloured Progressive Matrices[2]			
0	$17.0 \pm 5.4^{3,4}$	19.9 ± 6.3	
24 wk	$24.0 \pm 6.3^{4,5}$	20.5 ± 5.6	4.7 (3.8, 5.8)
Bead threading			
0	22.0 ± 3.5^{6}	22.9 ± 3.2	
			NS
24 wk	22.7 ± 2.8	23.1 ± 2.9	0.02 (−0.52, 0.55)
Rapid target marking[2]			
0	37.0 ± 12.6^{6}	34.2 ± 10.8	—
24 wk	$29.5 \pm 6.6^{4,5}$	31.0 ± 7.2	2.8 (1.6, 4.0)
Digit span forward			
0	7.7 ± 1.9	7.3 ± 1.9	
			NS
24 wk	8.0 ± 2.1	7.7 ± 2.0	0.006 (−0.36, 0.37)
Digit span backward			
0	4.3 ± 1.9	4.1 ± 1.6	
			NS
24 wk	4.5 ± 1.6	4.2 ± 1.5	0.23 (−0.075, 0.54)
Symbol search[2]			
0	17.3 ± 5.2^{4}	19.7 ± 4.8	
24 wk	$21.8 \pm 4.5^{4,5}$	20.5 ± 5.2	2.8 (1.9, 3.6)
Coding			
0	33.4 ± 9.4	33.4 ± 9.2	
			NS
24 wk	42.2 ± 9.8^{5}	41.8 ± 9.9^{5}	0.52 (−0.91, 1.96)
Rapid object naming[2]			
0	52.9 ± 15.1	49.9 ± 16.6	
24 wk	$42.5 \pm 10.6^{4,5}$	45.2 ± 13.5	4.5 (2.3, 6.6)

[1] Intervention was 400 mg I (as oral oxidized oil) or placebo.

[2] Significant differences by mixed-model ANOVA ($P < 0.0001$) after adjustment for baseline, school, and sex. Baseline values were used as a fixed effect.

[3] $\bar{x} \pm$ SD (all such values).

[4,6] Significantly different from control group (unpaired t test): [4]$P < 0.0001$, [6]$P < 0.05$.

[5] Significantly different from baseline, $P < 0.0001$ (paired t test).

involved in postsynaptic signaling (42). In the brain, expression of RC3 mRNA is reduced in hypothyroid animals and can be increased to normal levels by oral T_4 treatment (42). These findings suggest that circulating T_4 may be a good indicator of cerebral T_3 status. In the current study, the ≈40% increase in mean TT_4 after iodine treatment in children with poor baseline thyroid function may explain their improved test scores.

Four randomized controlled trials measuring the effect of iodized oil on cognition in children have been reported (11–14). The results are equivocal. Three of the studies found no effect (11, 13, 14), whereas one study found that cognition improved significantly with treatment (12). However, problems of method limit their interpretation. Two of the studies were confounded by a significant improvement in iodine status in the control group (11, 14), whereas, in the other 2, the treated group remained iodine deficient at retesting (12, 13). In iodine-deficient Bolivian children, no clearly beneficial effect of iodized oil on cognitive function was found, but there was a significant increase in UI concentrations in the control group (11). In Malawian children, iodized oil significantly improved performance on 1 of 3 motor tests and on all cognitive tests at 1-y follow-up. However, the baseline testing was unreliable, and the treatment group remained severely iodine deficient at time of retesting (12). Thyroid function was not measured in those 2 studies (11, 12). In

Malaysian children, no differences were seen in performance on a nonverbal intelligence test between treated and control children after 1 y of iodine supplementation, but iodine status improved in both groups (14). A study in Benin (16), planned as a 1-y randomized intervention with iodized oil, failed to produce clear results because the population began to use iodized salt during the intervention. The population was split post hoc, on the basis of changes in UI, into 2 subsets: a group whose iodine status was unchanged and a group whose iodine status improved. Although benefits were found in the group with improved iodine status, the study was not randomized, and T_4 concentrations improved to a significantly greater extent in the group with unchanged iodine status than in the group with improved status. In a well-controlled study in moderately iodine-deficient but euthyroid Bangladeshi children (13), treatment with oral iodized oil did not significantly improve cognitive or motor function at 4 mo. However, treatment did not normalize iodine status, and the iodine-treated children remained deficient at time of testing.

The strengths of the current study were a randomized, double-blind, placebo-controlled design; a large sample of children with marginal thyroid function; a remote study site to minimize risk of confounding from adventitious sources of iodine; and the use of a small number of carefully selected tests that were appropriate for the study population and that were administered under close

supervision. This study also has limitations. Despite randomization, there were group differences at baseline on 4 of the psychological tests, and a thorough analysis of the randomization scheme did not provide an explanation for this finding. However, these differences, although statistically significant, were small, and they were adjusted for in the statistical analyses. A further limitation was the modest test-retest reliabilities on 2 of the 7 tests (bead threading and symbol search), which may have reduced our ability to distinguish a treatment effect on these tests. Finally, the study was of short duration. A follow-up time of 24 wk was chosen to allow enough time to detect differences in test performance but not enough time to unduly delay iodine treatment in the control group, which included many children who had poor thyroid function because of iodine deficiency. Whether the observed improvement with iodine treatment would be sustained over a longer period is unknown.

We believe this study to be the first iodine supplementation trial to clearly show that the adverse effects of moderate iodine deficiency on aspects of cognitive and motor function in children are ameliorated and at least partially remedied with iodine repletion. Because impaired learning and reduced school performance adversely affect a region's development, productivity, and economic potential (2), these findings have particular relevance for policy makers and governments. They are generalizable in that the degree of iodine deficiency in our study population is present in many regions worldwide. They also support current recommendations from the World Health Organization for regional distribution of oral iodized-oil capsules to schoolchildren in areas of moderate iodine deficiency, as an interim measure, until salt iodization can be implemented (2).

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