The Benefits of Adequate Iodine Intake

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In past decades, researchers in various countries have studied the consequences of iodine deficiency on the mental and physical development of children and adults. Iodine deficiency proved to have disastrous consequences on cognitive and psychomotor development for a limited group (i.e., DeLong 1989). These are the so-called cretins, who make up more than 10% of the population in some areas. The World Health Organization estimates the worldwide number of overt cretins at around 5.7 million (Hetzell 1994).

Outcomes of study of the effects of iodine deficiency on the development of the noncretinous portion of a population living in an iodine-deficient area are less clear cut. While some studies pointed to a strong negative effect, little or no effect was found in others.

To obtain an overall picture of the current state of knowledge, the first part of this paper summarizes the results of a great many studies that have been performed in recent years. All these studies involved a comparison of the mental and psychomotor development in two groups of children and/or adults: (1) a non-iodine-deficient group — people living in a non-iodine-deficient area or children whose mothers were injected with iodized oil in the first part of their pregnancy; and (2) an iodine-deficient group — people living in an area with a serious iodine deficiency. Meta-analysis was used to combine the results of the studies.

In the second part of this paper, the outcomes are discussed of a recent study of the effect of iodine supplementation on the mental and psychomotor development of children born and raised in an iodine-deficient area in Malawi (Shrestha 1994). Although very little research has been done in this field, it is of great importance to know whether the negative effects of iodine shortage can be corrected at a later age through iodine supplementation.

Meta-analysis

The method of meta-analysis makes it possible to integrate the outcomes of a large number of studies on a single topic, resulting in a single overall estimate of the effect under study. This overall estimate is the average of the various outcomes weighted for sample size (Wolf 1986), whereby studies that used larger groups of subjects are ascribed more weight than studies performed on smaller groups.

This overall estimate, termed the “population effect size,” can be taken seriously only when the studies on which it is based meet the “homogeneity criterion”: the outcomes of the individual studies must not be too greatly divergent. Stoffelmayer et al. (1983) developed a measure for the degree of heterogeneity.

A meta-analysis consists of six steps: formulating the research issue, selecting the studies, coding characteristics of the studies, statistical analyses, interpreting the results, and drawing conclusions. The present study used the meta-analysis program of Schwarzer (1989).

Objectives

The objective of the meta-analysis is twofold. In the first place, it provides a highly complete summary of the research that has been performed in recent years on the relationship between iodine deficiency and mental and psychomotor development. Because the outcomes of the various studies are converted into the same measure, it is much
Table 1. Psychomotor ability: studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Country</th>
<th>n</th>
<th>Age (y)</th>
<th>Test</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td>250</td>
<td>6–12</td>
<td>Bender Gestalt Test</td>
<td>.48</td>
</tr>
<tr>
<td>Indonesia</td>
<td>143</td>
<td>6–12</td>
<td>Bender Gestalt Test</td>
<td>.37</td>
</tr>
<tr>
<td>Spain</td>
<td>97</td>
<td>2.5–5</td>
<td>McCarthy Motor Development Scale</td>
<td>.34</td>
</tr>
<tr>
<td>Zaïre</td>
<td>75</td>
<td>4–23*</td>
<td>Brunet-Lezine Scale</td>
<td>.30</td>
</tr>
<tr>
<td>Spain</td>
<td>78</td>
<td>6–8</td>
<td>Bender Gestalt Test</td>
<td>.29</td>
</tr>
<tr>
<td>Ecuador</td>
<td>264</td>
<td>8–18</td>
<td>Goddard Test for Psychomotor Development</td>
<td>.25</td>
</tr>
<tr>
<td>Chili</td>
<td>90</td>
<td>6–12</td>
<td>Bender Gestalt Test</td>
<td>.13</td>
</tr>
<tr>
<td>Spain</td>
<td>156</td>
<td>9–2</td>
<td>Bender Gestalt Test</td>
<td>.13</td>
</tr>
<tr>
<td>Bolivia</td>
<td>200</td>
<td>5.5–12</td>
<td>Bender Gestalt Test</td>
<td>-.01</td>
</tr>
<tr>
<td>Spain</td>
<td>74</td>
<td>2–30*</td>
<td>Bayley Scale of Infant Development (motor)</td>
<td>-.03</td>
</tr>
</tbody>
</table>

*Age in months.

Results

Table 1 shows the studies that focused on general psychomotor functioning. A total of 10 studies performed in seven different countries qualified for the meta-analysis. The test most frequently used was the Bender Gestalt test or adaptations of it (Koppitz 1975). A total of 1427 persons ranging in age from 2 months to 18 years were studied.

The effect sizes, given in correlation coefficients (r), showed much variation, from +.48 to -.03. The degree of homogeneity of the studies was determined using the index developed by Stoffelmayer et al. (1983). Together, the 10 studies did not meet the homogeneity requirement, which meant that they had not been performed on the same population.

When the two studies with a negative effect size, the studies in Spain and Bolivia, were omitted, the remaining eight studies, including 1153 individuals, were homogeneous. By transforming the outcomes into Fisher z-scores, an estimate could be made of the population effect size (weighted mean r). This was done using the Schmidt-Hunter method (Schwarzer 1989) in which different weights are ascribed to the various studies on the basis of the size of the groups studied. The weighted population effect size calculated was .30 (p<.00000), with a 95% confidence interval from .25 to .35 (see Table 2).

The studies relating to more specific factors within the psychomotor domain are shown in Table 3. Unfortunately, the number of these studies is limited, especially for the factors “speed of reaction” and “coordination of movements.”

As the seven studies involving research of manual dexterity formed a homogeneous group, it was not necessary to leave out any studies for the calculation of the overall effect size. The total number of individuals who took part in these studies was 1859. The weighted population effect size was .41 (p<.00000), and the 95% confidence interval was between .37 and .45.

The effect sizes calculated for the “speed of reaction” factor were quite divergent. The two studies in China showed the most extreme effect sizes of .74 and -.05, and they were consequently omitted in calculating the overall index. The weighted population effect size here was .26.
Table 2. Results of the meta-analyses for psychomotor and cognitive abilities

<table>
<thead>
<tr>
<th>Variables</th>
<th>General</th>
<th>Manual dexterity</th>
<th>Speed of reaction</th>
<th>Coordination of movements</th>
<th>Cognitive ability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of studies</td>
<td>8</td>
<td>7</td>
<td>3</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>Number of subjects</td>
<td>1153</td>
<td>1859</td>
<td>429</td>
<td>429</td>
<td>2214</td>
</tr>
<tr>
<td>Population effect size</td>
<td>.30</td>
<td>.41</td>
<td>.26</td>
<td>.11</td>
<td>.40</td>
</tr>
<tr>
<td>Significance</td>
<td>.000</td>
<td>.000</td>
<td>.000</td>
<td>.009</td>
<td>.000</td>
</tr>
<tr>
<td>Mean standardized difference</td>
<td>.66</td>
<td>.96</td>
<td>.55</td>
<td>.22</td>
<td>.90</td>
</tr>
<tr>
<td>95% confidence interval</td>
<td>.25−.35</td>
<td>.37−.45</td>
<td>.17−.35</td>
<td>.02−.20</td>
<td>.36−.43</td>
</tr>
</tbody>
</table>

with a 95% confidence interval from 0.17 to 0.35.

The three studies relating to the “coordination of movements” factor yielded an overall effect size of 0.11 and a 95% confidence interval from 0.05 to 0.20.

Table 4 summarizes the 21 studies on the relationship between iodine deficiency and cognitive development. To obtain a homogeneous group of studies, the three studies with the smallest effect sizes were not used for meta-analysis. The effect sizes for the remaining 18 studies, with a total of 2214 individuals, ranged from 0.18 to 0.57. The weighted population effect size was 0.40 (significant at p<0.00000), with a 95% confidence interval from 0.36 to 0.43.

Figure 1 shows all effect sizes with the corresponding 95% confidence intervals.

Effects of Iodine Supplementation

So far, very little research has been done of the effects of iodine supplementation on mental and psychomotor development of people living in an iodine-deficient area. A few years ago, one such study was started by the Department of Human Nutrition of Wageningen Agricultural University. The study, doctoral research by Ramesh Shrestha, was performed in the Ntcheu district in Malawi, an iodine-deficient area where 86% of the children “were at least moderately iodine-deficient with urinary iodine concentrations below 0.4 μmol/L and 18% were anemic (blood hemoglobin concentration <110 g/L)”. The Free University of Amsterdam and the Tilburg University, both in the Netherlands, were also involved in this study.

Study Design

The research group consisted of a total of 321 children aged from 6 to 8 years from three primary schools. The children were divided into four groups that were controlled for school class, age, and sex:

1. placebo group (n=82)
2. iodine-supplemented group (n=79)
3. iron-supplemented group (n=78)
4. iodine- plus iron-supplemented group (n=82)

This publication will report outcomes only from the study of the first two groups of children, the placebo group and the iodine-supplemented group.

Both groups of children were given a large number of tests to determine their cognitive and psychomotor skills. The tests were administered twice: immediately before the children were given iodized oil and poppyseed oil, and 10 months afterward. As it was a double-blind study, the teachers and the researchers learned only after the tests were administered for the second time which children had been treated with iodine and which children had been in the placebo group.

Test Battery

Psychomotor abilities. The following tests were selected to study the psychomotor aspects:
Table 4. Cognitive ability: studies included in the meta-analyses

<table>
<thead>
<tr>
<th>Country</th>
<th>n</th>
<th>Age (y)</th>
<th>Test</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indonesia</td>
<td>102</td>
<td>13–20</td>
<td>Test Intelligensi Kollektip Indonesia</td>
<td>.57</td>
</tr>
<tr>
<td>New Guinea</td>
<td>20</td>
<td>10–12</td>
<td>Pacific Design Construction Test</td>
<td>.56</td>
</tr>
<tr>
<td>Spain</td>
<td>97</td>
<td>2.5–5</td>
<td>McCarthy Scales of Children’s Abilities</td>
<td>.53</td>
</tr>
<tr>
<td>China</td>
<td>499</td>
<td>7–14</td>
<td>Combined Raven’s Test for Rural China.</td>
<td>.51</td>
</tr>
<tr>
<td>Ecuador</td>
<td>32</td>
<td>3–5</td>
<td>Stanford-Binet Intelligence Scale</td>
<td>.50</td>
</tr>
<tr>
<td>Ecuador</td>
<td>46</td>
<td>6–10</td>
<td>Goodenough Draw-a-Man Test</td>
<td>.48</td>
</tr>
<tr>
<td>Ecuador</td>
<td>67</td>
<td>3.5–5.5</td>
<td>Stanford-Binet Intelligence Scale</td>
<td>.48</td>
</tr>
<tr>
<td>Spain</td>
<td>184</td>
<td>6–12</td>
<td>Cattell Culture Fair Intelligence Test</td>
<td>.45</td>
</tr>
<tr>
<td>Ecuador</td>
<td>124</td>
<td>3.5–5.5</td>
<td>Stanford-Binet Intelligence Scale</td>
<td>.37</td>
</tr>
<tr>
<td>Indonesia</td>
<td>143</td>
<td>6–12</td>
<td>Test Intelligensi Anak</td>
<td>.36</td>
</tr>
<tr>
<td>Spain</td>
<td>74</td>
<td>2–30a</td>
<td>Bayley Scale of Infant Development</td>
<td>.36</td>
</tr>
<tr>
<td>China</td>
<td>192</td>
<td>7–14</td>
<td></td>
<td>.28</td>
</tr>
<tr>
<td>Indonesia</td>
<td>163</td>
<td>5–20</td>
<td>Raven Coloured Progressive Matrices</td>
<td>.28</td>
</tr>
<tr>
<td>Zaire</td>
<td>138</td>
<td>4–23a</td>
<td>Brunet-Lézine Scale</td>
<td>.26</td>
</tr>
<tr>
<td>Chili</td>
<td>90</td>
<td>±6–±12</td>
<td>Wechsler Intelligence Scale for Children Rev.</td>
<td>.20</td>
</tr>
<tr>
<td>China</td>
<td>94</td>
<td>0–7</td>
<td></td>
<td>.18</td>
</tr>
<tr>
<td>Ecuador</td>
<td>108</td>
<td>12–15</td>
<td>Wechsler Intelligence Scale for Children</td>
<td>.12</td>
</tr>
<tr>
<td>Ecuador</td>
<td>154</td>
<td>8–12</td>
<td>Stanford-Binet Intelligence Scale</td>
<td>.08</td>
</tr>
<tr>
<td>Bolivia</td>
<td>200</td>
<td>5.5–12</td>
<td>Stanford-Binet Intelligence Scale</td>
<td>.04</td>
</tr>
</tbody>
</table>

Source: Bleichrodt and Born (1994).

* Age in months.

Figure 1. Visual display of effect sizes and confidence intervals for 10 studies concerning psychomotor ability and 21 studies concerning mental ability.
1. Pegboard: inserting pegs into holes as quickly as possible
2. Tapping: tapping two hatched rectangular plates with a pencil as rapidly as possible
3. Throwing balls: throwing balls into a basket from a fixed distance
4. Balancing: standing on each foot for as long as possible with a maximum of three minutes
5. Sitting/standing: sitting down and standing up as many times as possible in one minute
6. Reaction time: pressing a button as soon as a small square appears on a screen and a beep is heard
7. Handgrip: hand muscle strength measured by means of a hand dynamometer

The same or comparable tests have been used in previous research of the effects of iodine deficiency on psychomotor development. Although the test battery does not represent the full spectrum of the psychomotor domain, it does cover important aspects such as finger and manual dexterity, eye-hand coordination, reaction time, and coordination of movements.

Cognitive abilities. The choice of the tests to determine cognitive abilities was based on the nonhierarchical multifactor model of Thurstone (1938). Even today, the factors identified by Thurstone — verbal, numerical, spatial, perceptual, word fluency, memory, and reasoning — are still considered to be important distinctions in intelligence theory, and they are therefore represented in many test batteries. This also applies to the test battery used for the research in Malawi. The test battery consisted of six subtests:

1. Fluency: giving as many names of persons and animals as possible within a certain time limit
2. Exclusion: indicating which of four objects or abstract figures does not satisfy the same condition as the other three
3. Quantity: making comparisons in number, volume, length, distance, weight, surface area, etc., on the basis of drawings
4. Verbal meaning: from four pictures, choosing the one that corresponds to the word named by the tester
5. Visual memory: recognizing a figure shown earlier among a group of several figures
6. Closure: recognizing objects which are shown in an incomplete fashion

Previous study has shown that the psychological meaning of the above tests is comparable for different cultures.

On the basis of the six subtest scores a total score was calculated as an indication of overall cognitive functioning. However, the reliability of the individual subtests also allowed their separate analysis and interpretation.

Results
Figure 2 shows the differences in test scores between the iodine-deficient or placebo group and the non-iodine-deficient or treated group. The differences are expressed as d-values. The d-value is the difference between the means of the two groups divided by the standard deviation. Cohen (1988) divided the d-values into three categories: small effect size (d=0.2), medium effect size (d=0.5), and large effect size (d=0.8).

The outcomes of the research of the effects of iodine supplementation on psychomotor development in the children studied were not clear-cut. For skills measured by the subtests Pegboard, Tapping, Balancing, and Reaction time, the effects were negligible. A medium effect size was found for Throwing balls, while a large effect size was found for Handgrip and, even more pronounced, for Sitting/standing.

The outcomes for the mental abilities were clearer. With the exception of the subtest Verbal meaning, with a d-value of zero, positive d-values were found, ranging from medium effect sizes for Exclusion, Quantity, and Closure to large effect sizes for Fluency and Visual memory.

Together the six subtests give a reliable indication of the general cognitive functioning of the children. The d-value of 1.24 is very high: concretely, it means a difference of 1.24 SD or 18 IQ points between the group that received supplemental iodine and the placebo group. If the extremely high d-value for Fluency is left out, the other five subtests still show a d-value of 0.75, or a difference of 11 IQ points.

Conclusion and Discussion
There is great variation in the outcomes of the studies that focused on psychomotor skills. Even when the same test was used, the effect sizes found differ greatly from study to study; for example, the correlation coefficients for the...

Figure 2. Differences in test scores between the iodine-treated group and the placebo group expressed in d-values.

<table>
<thead>
<tr>
<th></th>
<th>treated group</th>
<th>placebo group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MENTAL ABILITY</strong></td>
<td>lower</td>
<td>higher</td>
</tr>
<tr>
<td>Fluency</td>
<td></td>
<td>2.94</td>
</tr>
<tr>
<td>Exclusion</td>
<td></td>
<td>0.56</td>
</tr>
<tr>
<td>Quantity</td>
<td></td>
<td>0.41</td>
</tr>
<tr>
<td>Verbal meaning</td>
<td></td>
<td>0.00</td>
</tr>
<tr>
<td>Visual memory</td>
<td></td>
<td>0.91</td>
</tr>
<tr>
<td>Closure</td>
<td></td>
<td>0.43</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1.24 (18 IQ pts)</td>
</tr>
<tr>
<td>Total (excl. Fluency)</td>
<td></td>
<td>0.75 (11 IQ pts)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>PSYCHOMOTOR ABILITY</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pegboard</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>Tapping</td>
<td>-0.09</td>
<td></td>
</tr>
<tr>
<td>Throwing balls</td>
<td>0.45</td>
<td></td>
</tr>
<tr>
<td>Balancing</td>
<td>-0.16</td>
<td></td>
</tr>
<tr>
<td>Sitting/standing</td>
<td>4.10</td>
<td></td>
</tr>
<tr>
<td>Reaction time</td>
<td>-0.11</td>
<td></td>
</tr>
<tr>
<td>Hand grip</td>
<td>0.81</td>
<td></td>
</tr>
<tr>
<td><strong>d-values</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluency</td>
<td>2.94</td>
<td></td>
</tr>
<tr>
<td>Exclusion</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Quantity</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>Verbal meaning</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Visual memory</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>Closure</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1.24 (18 IQ pts)</td>
<td>0.75 (11 IQ pts)</td>
</tr>
</tbody>
</table>

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Bender Visual Motor Gestalt Test vary from -.01 to .48 and for the Reaction time test from -.05 to .74. However, the group of subjects with an iodine deficiency obtained lower scores than the group that did not suffer from an iodine deficiency in nearly all studies.

Table 5. Summary meta-analyses and Malawi study

<table>
<thead>
<tr>
<th>Test</th>
<th>Meta-analysis (d-value)</th>
<th>Malawi study (d-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychomotor ability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>.66</td>
<td>.25</td>
</tr>
<tr>
<td>Manual dexterity</td>
<td>.96</td>
<td>.07</td>
</tr>
<tr>
<td>Speed of reaction</td>
<td>.55</td>
<td>-.11</td>
</tr>
<tr>
<td>Coordination of movements</td>
<td>.22</td>
<td>.29</td>
</tr>
<tr>
<td>Muscle strength</td>
<td>—</td>
<td>2.46</td>
</tr>
<tr>
<td>Cognitive ability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>.90</td>
<td>1.24</td>
</tr>
<tr>
<td>(13 IQ points)</td>
<td>(18 IQ points)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.75</td>
<td>(11 IQ points)</td>
</tr>
</tbody>
</table>

*a* Difference between iodine deficient/non-iodine-deficient.  
*b* Effect of iodine supplementation.  
*c* Excluding Fluency.

Table 5 summarizes the outcomes of the meta-analyses and Malawi study. The highest difference was found for skills requiring manual dexterity (Pegboard, Tapping), for which a high d-value of 0.96 was found (large effect size). For the factor of Reaction time and for general psychomotor functioning, d-values were found of 0.55 and 0.66 respectively (medium effect size).

Assuming that the outcomes of the meta-analyses are reliable, then on the basis of the outcomes of the Malawi study, we must conclude that the disorders in psychomotor functioning that are caused by an iodine deficiency cannot be corrected, at least not within the 10 months that the study lasted in Malawi. The differences between the group that was treated with iodine and the nontreated (placebo) group are negligible; the d-values for the psychomotor skills range from -0.11 to 0.15. Iodine supplementation seems to give an improvement only for the factor of muscle strength, where a large effect size was found.

The studies that focused on the influence of iodine deficiency on cognitive development yield a fairly straightforward picture. The correlation coefficients vary from .04 to .57, with a median of .36. The d-value is 0.90 (large effect size), which means a difference of 13 IQ points between the iodine-deficient and the non-iodine-deficient group. However, from the results of the study in Malawi, we may conclude that iodine supplementation can make up for developmental lag of the iodine-deficient group within a year: the d-value of 1.24 found for general cognitive ability implies that the average test score of the treated group is roughly 18 IQ points higher. Even when the subtest most susceptible to environmental factors, Fluency, is omitted, a considerable difference of 11 IQ points remains between the two groups.

The remarkable outcomes of both the meta-analysis and the Malawi study point to the need for further research. Some factors that will require special attention are the choice of the research groups, the selection of the test instruments, and the control of the conditions under which the tests are administered.

As much as possible, test batteries for both psychomotor skills and cognitive skills must be composed of tests that are culture fair. When the tests are administered, much attention should be paid to aspects such as standardization and objectivity. Administering the same test in several different countries will yield important information on the effects of iodine deficiency on psychomotor and cognitive development and the effects on development if iodine is administered at a later age.

Acknowledgment

We thank Dr. P.H. Dekker for his valuable contribution to the statistical analysis of the data.

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