Vitamin/Mineral Supplementation and the Intelligence of Children — A Review

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Abstract

Seven studies are reviewed that have examined the impact of vitamin/mineral supplementation on children's performance on intelligence tests. Five studies have reported that the taking of supplements was associated with improved performance, although not all children respond, rather those whose diet supplies low levels of vitamins and minerals benefit. In the studies that have reported positive findings, in each case the response was primarily in terms of non-verbal measures of intelligence, a change that is predicted theoretically. There have been suggestions that supplementation may also be associated with an improved mood and the ability to sustain attention, although it is unclear whether this completely accounts for the improved performance on non-verbal intelligence tests.

Introduction

Conventional nutritional wisdom suggests that for the vast majority of the population the intake of micro-nutrients is not a matter for concern. The argument goes that if the diet supplies sufficient protein and calories, then the necessary vitamins and minerals come associated with the protein and calories. Evidence supporting a conflicting view will be discussed, that a sub-clinical deficiency of micro-nutrients exists in some children to the extent that psychological functioning is disrupted. To this end seven recent studies of the impact of vitamin/mineral supplementation on the intelligence of children will be described and discussed.

Study One — Benton and Roberts[6]

Sixty children were matched by their teacher for sex, school performance, and home background. Randomly, and under a double blind procedure, they were allocated to groups that received either a placebo or a multi-vitamin/mineral supplement. After taking the supplement for eight months the scores on the Calvert non-verbal intelligence test increased by nine points, whereas when taking the placebo the scores increased by 1.8 points ($p < 0.0010$). The verbal intelligence scores of those taking the two types of tablet were not significantly different.

The response was immediate, angry and dismissive[15] to which Benton[1] replied. It is essential to distinguish two parts of this study, the intervention trial and the dietary analysis. Strangely, as the letters to the *Lancet* wished to dismiss the intervention trial, they made few comments about the part of the study that had produced the unexpected increase in nonverbal intelligence. In fact virtually all comments were directed to a dietary survey that is not relevant in the present context. The only substantive comment on the major part of the study concerned statistical analysis, these concerns were answered.[1] In addition, at the request of the British Medical Research Council Committee set up to examine this topic, the raw data were made available to one of their statisticians who confirmed that the non-verbal intelligence of the group who took the supplement had increased significantly more than those receiving the placebo.

It is very safe to assume that the angry letters to the *Lancet* would have pointed out any flaws in the design of the Benton and Roberts[6] study — they did not. We are left with a study that used a widely accepted protocol for clinical drug trials that produced an unexpected finding. In such cases the possibility that the result was a statistical freak has to be considered seriously (although the probability against this was one in a thousand). The authors were aware of this and were cautious in their conclusion, their final comment was that; "Clearly the study must be replicated ...": it was equally unclear whether the result reflected some unusual characteristics

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of the sample, rather than a more general phenomenon.

Study Two — Schoenthaler et al[23]

At the same time as the Benton and Roberts[6] study was being carried out a similar study was in progress in the United States, although it was published much later. Schoenthaler et al[23] studied twenty-six delinquent juveniles, aged between 13 and 16, who under a double blind procedure were randomly allocated to groups receiving either a placebo or a multi-vitamin/mineral supplement for 13 weeks. Intelligence was assessed using the Wechsler Intelligence Scale for Children — Revised (WISC-R).

No significant change in verbal scores resulted. The intelligence scores of those receiving the placebo decreased by an average of one point whereas when taking the supplement it increased by six points ($p < 0.05$). Before and after taking the tablets blood samples were taken and used to assay ten vitamins and seven minerals. Individuals were distinguished whose levels of blood micro-nutrients had, or had not, increased. A decrease in the non-verbal intelligence of 2.7 points was found in those whose blood micro-nutrients status had not changed while taking the tablets, whereas in those whose blood status had improved there was an increase of 11.6 points ($p < 0.001$).

The report of Schoenthaler et al[23] lacks important details. Details of the biochemical assays are not given and definitions of unchanged and improved levels of blood vitamins are not stated. Although probabilities are given in the text, the nature of the statistical analysis is not reported, so it is not possible to judge whether it was appropriate.

Study Three — Nelson et al[17]

The race started to demonstrate that the phenomenon did not exist. The Nelson et al[17] study examined fifty-one children aged 7-10, and one hundred and seventy-six children aged 11-12, who were matched by sex and age. They were then randomly, and under a double-blind procedure, placed into groups that took either a multi-vitamin/mineral supplement or a placebo. Intelligence tests were administered before and after taking the tablets for four weeks. The younger children completed the Heim AIX test of non-verbal intelligence, while the older children completed the Heim AH4 test of verbal and nonverbal intelligence. All children completed the WISC-R digit span and coding tests. "On retesting there were no significant differences in the performance" of those taking the placebo and active tablets. The authors conclude that they "... found no evidence that learning ability in a cross-section of British school children was limited by the quality of their diets".

The study differed from Benton and Roberts[6] in many ways making it difficult to compare the findings.[19] It used different tests, different tablets, and took them for a much shorter period. Schoenthaler et al[24] produced data that readily accounts for the negative findings of Nelson et al.[17] After a month Schoenthaler et al[24] found a significant increase in non-verbal scores (Ravens Matrices) in those children who received tablets containing twice, but not once, the U.S. Recommended Daily Amount (RDA); Nelson et al used once the UK Rias (the UK Rias are generally lower than the U.S. Rias). Schoenthaler et al[24] suggested that the negative data of Nelson et al[17] reflected the use of too small a dose for too short a period.

In the Nelson et al[17] study there was a significant difference in the non-verbal intelligence of the younger children before taking the tablet. Such a demonstration that the samples were not matched in a satisfactory manner makes the data from the 7-10 year old children of little value. The analysis of the impact of supplementation took no account of nutritional status. Attempts were made to relate the intake of various vitamins to test performance using regression equations. As few people would expect a linear relationship between vitamin status and psychological functioning this type of analysis was obviously inappropriate. The most commonly quoted hypothesis in this area, that there is a sub-group of badly nourished children that respond, was not explored. Nelson et al[17] simply asked if all children would respond, the conclusion that they do not is universally accepted.

Study Four — Crumb et al[10]

Initial intelligence test scores of eighty-six 11-13 year old children were used to produce a stratified sample that was then randomly, and under a double-blind procedure, allocated

to groups receiving a placebo or the same supplements as in the Benton and Roberts[6] study. The same tests as the Benton and Roberts[6] study were used and in addition the Cattell culture-fair test, Ravens' standard progressive matrices and AH4 part II, were administered before and after taking the tablets for seven months.

The authors state "A small, non-significant difference between the control and supplementation groups was found in a non-verbal test. The net difference in changes in scores between the active and placebo groups was 2.4 units". The "... study does not support the hypothesis that vitamin and mineral supplementation leads to improved performances in non-verbal tests of reasoning".

Crumb et al[10] tried to faithfully replicate the Benton and Roberts[6] design in a way that Nelson et al[17] had not; in this respect it must be viewed as potentially producing valuable data. However, the failure of this study to include gender as a factor in the analysis of variance is a cause of great concern: gender differences in non-verbal intelligence have been repeatedly reported and Benton and Buts[4] found that only boys responded in their sample. It turns out that there were many more girls than boys in the Crumb et al[10] study, although this may not be a problem as most studies have found that both girls and boys respond to supplementation.

Although Crumb et al[10] used a seven day dietary diary to estimate the intake of micronutrients, they failed to relate diet to any response to supplementation. Again the only question asked was do all children respond. The answer no is uncontroversial but the question remains as to whether a sub-group of poorly fed children responded. In a letter to *Lancet*[11] they reported that only six percent of their children were as badly nourished as the children who responded in the Benton and Buts[4] study in Belgium. The possibility remains that the response to supplementation in a few children may have been hidden by the lack of response of the majority.

Study Five — Benton and Buts[5]

A group of 167 thirteen year old children were studied in seven schools in Belgium. Under a double-blind procedure they were randomly allocated to groups that received either a placebo or a multi-vitamin/mineral supplement for five months. Supplementation failed to influence the verbal scores. Diet was assessed using a fifteen day dietary diary and a group of about a third of the boys was selected who consumed significantly less of 10 micronutrients, although broadly the same macro-nutrients as the rest of the sample. Neither the girls, nor the boys whose diet supplied higher levels of micro-nutrients, responded to supplementation. However, the non-verbal intelligence of the boys who ate the poorer diet, and received the supplement, increased by six points, whereas the scores of those receiving the placebo decreased by three points ($p < 0.02$).

The majority, but not all the boys who responded to supplementation, were in schools for the less academically able children. Benton[2] calculated that the diets of the Belgium children who responded were significantly worse, in terms of the micro-nutrients offered, than the diets of the children in both the Nelson et al[17] and Crumb et al[10] studies. The fact that the vast majority of the boys who responded in the Benton and Buts[4] study were from two of the seven schools studied illustrates that the choice of subjects is critical. Had the other five schools been studied exclusively, then no response would have been reported.

The failure of girls to respond in the Benton and Buts[4] study is an unusual finding that is not easily explained. Other studies reporting positive findings have not found it to be an exclusively male characteristic. The authors speculated that the fact that the diets of the two groups of Belgium girls were not so extreme as the boys might have been important.

A second line of argument was that gender differences in the attitudes to schooling may have played a part. Both explanations need to be further examined before drawing a firm conclusion.

Study Six — Schoenthaler et al[24]

The largest and most controversial study in this series was carried out in California and involved six hundred and fifteen school children, aged 12-13 and 15-16 years. Under a double-blind procedure, they were randomly allocated to groups who received a placebo, or an active tablet that contained twenty-three micro-nutrients at a strength of either 50%, 100% or 200% of the US RDA. Various tests were administered before and after taking the

tablets for three months; WISC-R; Matrix Analogies Test; Reaction Time and Inspection Time test; Comprehensive Test of Basic Skills; Ravens Matrices (after four weeks only).

The authors state that the "Results showed that for non-verbal Wechsler Tests there were highly significant improvements in I.Q., whereas for verbal tests there were none". The improvements were associated with the taking of the 100% RDA tablets rather than the 50 or 200% of the RDA. The non-verbal scores of those taking the placebo increased by 8.9 points whereas the increase was 12.6 points when the 100% RDA tablets were taken ($p < 0.001$). No significant differences were reported for the various group administered intelligence tests, something explained as a reflection of the poor cooperation of the school-children. "Responders" were defined as those whose intelligence scores had increased by 15 points or more, whereas those whose scores increased by seven points or less were labelled "non-responders". By this definition 45% of those taking the 100% RDA tablets were "responders" and 55% "non-responders"; the implication is that improvements in intelligence scores were concentrated in a sub-group deficient in vitamins and minerals. Cole and Whitehead[9] argued that if there was a group of responders then the standard deviation should be greater when taking the tablets, something they suggest did not occur. They also note that it was surprising that a response was found equally in all four schools examined; as some schools were in economically depressed and some in privileged areas, an equal response was unlikely.

In several places the paper lacks important details that makes it difficult to evaluate.[7] Details of the statistical analysis used are missing although the analysis was carried out blind by a medical statistician recruited for the purpose. There is no evidence presented that those who finished the trial were similar to those who started: the concern is that there was a differential drop out in the four groups that systematically changed the scores at the end of the study. Both Blinkhorn[7] and Peto[16] commented on the number of statistical comparisons that were possible in the study, such that it was likely that one occurred by chance. Schoenthaler[20] denied that many of the comparisons suggested by Peto had in fact been made and Benton[3] commented that the change in non-verbal intelligence was predicted theoretically, and as it had been found in five studies (see below), it was difficult to explain this selective and consistent impact on intellectual functioning as a statistical freak. This study is the only one that has used more than one dose; the finding that only the 100% RDA tablets produced significant results is perplexing. The taking of the 200% RDA tablets was associated with non-verbal scores significantly worse than when taking the 100% RDA tablets, although results with this highest dose did not differ from the placebo. The results implied that there is a critical intake of micronutrients. Although a high intake of some vitamins is known to be associated with toxicity, that 100% RDA is such a critical level of intake, and that 200% RDA was detrimental, was unexpected.

The paper states that more positive data will be published from this study, however, the veracity of this claim awaits the opportunity to study the methodology. A footnote to the paper says "A smaller replication of this study was carried out in Great Britain, under the supervision of Dr. D. Tamir of Jerusalem. Results were generally supportive of those reported here and will be published in due course". Although details are not given, on the basis of a preliminary analysis the authors say: "the supplements produced significant changes in blood nutrients concentrations for selected vitamins and minerals; responders had significantly different changes in blood nutrient concentrations than non-responders; and responders were more likely to have low blood nutrient concentrations in the pre-test". The authors stress that these comments should be treated as preliminary and are in need of more scrutiny, in fact no supporting evidence has been presented at this stage.

Study Seven — Benton and Cook[5]

On the basis of the previous findings, both positive and negative, Benton and Cook[5] argued that a response to supplementation would only be expected in poorly fed children. Six year olds were studied as, judging by parental comments, this is an age when feeding is a particular problem. Forty-seven children, aged 6 and a half years, were randomly allocated to one of two groups that received either a multi-vitamin/mineral supplement or a placebo,

under a double blind procedure. Before and after six weeks of taking the tablets in one school, and eight weeks in another, the children took four sub-tests of the British Ability Scale. A food frequency questionnaire was used although such an approach offers at the best a crude measure of diet.

When an overall intelligence score was calculated the scores of those taking the supplement increased by 7.6 points, whereas taking the placebo was associated by a fall of 1.7 points ($p < 0.007$). When the sub-tests were examined marked changes in non-verbal rather than verbal tests were found. When taking the active tablets non-verbal scores increased by 10.8 points compared with an increase of 1.3 when taking the placebo. The response to supplementation was greater in a school from an economically deprived rather than more affluent area. Supplementation increased the ability of children to concentrate when performing a computer game that was too difficult for children of this age. In a second test of attention supplementation improved the performance of girls but not boys.

Discussion of the Seven Studies

Psychological measures have been used relatively infrequently to study the adequacy of diet. However, cognitive functioning involves the summated activity of many billions of neurones, and countless biochemical pathways and their associated enzymes. It may well be that relatively small dietary deficiencies, that are dismissed as causing only minor changes to the activity of a single enzyme, will along with many other similar minor effects, have a measurable and potentially important cumulative influence on cerebral functioning. As such, psychological measures may prove to be a means of demonstrating sub-clinical deficiencies of micro-nutrients.

Non-verbal Intelligence

In the seven studies described above the pattern of changes following supplementation is remarkably constant. On all five occasions when an improvement in intelligence has been reported, non-verbal rather than verbal measures have changed.[4 5 6 23 24] The consistency of the selective change in non-verbal scores is of great theoretical significance. Verbal intelligence reflects educational and other experience; it is a measure of achievement. Non-verbal ability is thought to measure potential, it is a reflection of basic biological functioning.[6] If supplementation was to facilitate basic biology then *a priori* you would predict that non-verbal scores would be influenced.

The consistency of the change in non-verbal intelligence makes it difficult to dismiss these data. Anybody trying to explain away these data have the difficult job of explaining this consistent and selective impact on intellectual functioning. The pattern of change is predicted theoretically; it is impossible to achieve by any known pharmacological means; it has been repeatedly found in studies that use slightly different experimental designs making it difficult to explain as the product of a common methodological fault.

Attention

Benton[2] suggested that, in part at least, the response to supplementation may reflect improved attention. When intelligence tests are taken on a second occasion an improvement in performance is expected as the task is familiar. On four out of the five occasions when improved intelligence scores have resulted from supplementation, the performance of those taking the placebo has either declined, or at least not increased in the expected manner.[4 5 6 23] The children would not be expected to become less intelligent over a few weeks; a problem of concentration or attitude would explain this profile.

Benton and Cook[5] specifically tested the attentional deficit hypothesis; they found that the taking of supplements increased the time that children spent concentrating, when trying to perform a difficult computer game at which they inevitably failed. On a second task there was some evidence that the attention of girls, but not boys, was improved by supplementation. As the improvement in non-verbal intelligence was similar in both sexes in this study, it is unlikely that attentional deficits entirely explained the findings.

The Schoenthaler et al[24] study is the exception. In those taking the placebo, non-verbal intelligence increased by nine points, almost exactly that which the manual of the WISC-R says is to be expected on taking the test for a second time. As fifty-five percent of those in

this study were said to be non-responders it may be that in part the increased non-verbal scores of those taking the placebo reflected the expected improvement of the majority who were well nourished.

Kerimova and Aleskerova[23] examined a group of 120 six year olds in Azerbaijan whose vitamin intake was 25 to 60% of the recommended level. Those receiving a vitamin supplement for six months were found to have "significantly lowered fatigue ... the working capacity and attention as well as nervous-reflectory activity were significantly improved ..."

Mood

Schoenthaler[21] studied young offenders, guilty of serious crimes, in two penal institutions. He used a seven day dietary diary to distinguish those who were well nourished (43%) from those with deficiencies (57%) of minerals and vitamins. A multi-vitamin and mineral supplement was given for three months to all offenders, irrespective of the quality of their diet: it was argued that those with a poor diet would respond, while the well nourished would not. In one institution a mood scale was administered and it was found that, when compared with those eating an adequate diet, the mood of those with a poor diet improved over the course of the experiment ($p < 0.01$). In a second penal institution, in those having a poor diet, the taking of a supplement decreased misbehavior by 69% ($p < 0.05$). Although this type of study can suggest mechanisms, the fact that subjects are not randomly allocated to treatments, makes it possible that due to self selection the two groups were unmatched.

Schoenthaler et al[22] randomly allocated 71 residents in a juvenile treatment facility to groups receiving either a placebo or a vitamin/ mineral supplement. The taking of the active tablets was associated with a significant fall in the incidence of violence recorded by staff under double-blind conditions ($p < 0.009$). Heseker et al[12] screened 1228 male subjects aged 17 to 29 for low levels of blood vitamins and selected 197 who received, under a double blind procedure, supplements or a placebo for eight weeks. The taking of the supplement was associated with improvement on several indices of mood.

Adequacy of Diet

There are several suggestions that a response to supplementation is to be expected in only some children. Benton and Buts[4] used a dietary diary to distinguish a group of a third of the boys whose diets supplied fewer micronutrients than the rest of the sample. It was the sub-group with the poor diet whose non-verbal intelligence increased. Schoenthaler et al[23] found increases in non-verbal intelligence only in those whose levels of blood micro-nutrients increased following supplementation. Schoenthaler et al[24] found that although there was an overall average increase in non-verbal intelligence, in fact there was a relatively large increase in 45% of the sample, and a limited response in the rest. Preliminary data suggested that those who responded had lower levels of blood vitamins and minerals than those who did not respond.

Benton and Cook[5] used a food frequency questionnaire to make a crude estimate of the content of dietary sugar in the diets of their sample of six year olds. There was a significant correlation between the amount of sugar in the diet and the increase in intelligence when taking supplements ($p < 0.004$); that is the more sugar in the diet the greater was the response to vitamin/mineral supplements. The relevance of this correlation is that sugar offers calories associated with only very small amounts of vitamins and minerals, suggesting that a greater response occurred in those whose diets provided fewer vitamins and minerals. This correlation between the response to supplementation, and the estimate of sugar in the diet, suggests a hypothesis concerning the origin and solution of the problem. Lest et al[14] reported that the proportion of refined carbohydrate in children's diet was negatively correlated to intelligence and school performance.

Additional support for the implication that children who take too many of their calories in the form of sugar may be deficient in vitamins and minerals comes from a study of Nelson and Paul[16] In adults they found that there was a trend for the intake of micro-nutrients to be lower in those consuming higher amounts of sugar; the micro-nutrient intake was found to be particularly low in those consuming a low energy diet where a high proportion of energy came in the form of sugar. Although any extrapolation from adults to six year old chil-

dren should be made with caution it may be that young children, whose attitudes to eating are characterized by fads, lack of appetite, or a battle of will with the parents, may have a low calorie diet where too high a proportion of calories come in the form of sugar with its innately attractive sweet taste.

Conclusions

1) The hypothesis should be considered that the diet, of some but not all children, is such that a sub-clinical deficiency of vitamins and minerals exists to the extent that psychological functioning is adversely influenced. Clearly a firm conclusion awaits further evidence. In particular studies that use biochemical assays of vitamin status will be important. We await evidence that a response is only found in those with a poor vitamin status that improves following supplementation.

2) The possibility that high risk groups exist should be considered. These might be characterized on the basis of age, eating habits, social background, psychological or behavioral problems.

3) Given their widespread neural importance it is unlikely that a sub-clinical deficiency of vitamins and minerals will be associated with only one aspect of psychological functioning. Future research should consider a range of possible influences including the ability to sustain attention, mood and intellectual ability.

4) The effects of rectifying a sub-clinical deficiency are likely to be gradual rather than sudden, subtle rather than dramatic. The benefits of an optimally functioning neuroche-mistry will only be realized if the individual is in a stimulating and emotionally secure situation in the presence of those with favorable attitudes.

5) There is little doubt that many in the population will find very attractive an apparently simple solution to their children's problems. However, sub-clinical deficiencies are likely to be at the most a small part of the cause of psychological problems of some children. Even in this minority of children, supplementation in itself is unlikely to offer a complete solution. At the most diet is only one factor, amongst many others, that modulates behavior.

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