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Vitamin–mineral supplements and intelligence

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Seven studies, using the double-blind placebo-controlled design that is expected in clinical trials, have examined the impact of vitamin–mineral supplementation on children's performance in intelligence tests. Of these, five have reported that the taking of supplements was associated with improved performance by some children (Benton & Roberts, 1988; Benton & Buts, 1990; Benton & Cook, 1991*a*; Schoenthaler *et al.* 1991*a*,*b*), whereas two report negative findings (Crombie *et al.* 1990; Nelson *et al.* 1990). As the strengths and weaknesses of these studies have been debated elsewhere the present paper will address other questions (Benton, 1988, 1991*a*; Letters, 1988; Rippere, 1988; Blinkhorn, 1991; Cole & Whitehead, 1991; Peto, 1991; Schoenthaler, 1991). The present paper, after commenting about the impact of vitamin–mineral supplementation on children, examines a more general question: 'Is it likely that sub-clinical deficiencies of micronutrients exist in Western industrialized societies to the extent that psychological functioning is disrupted?' This general question is important because much of the scepticism and controversy which surround the reports that the intelligence scores of some children respond to supplementation, reflects the certainty that sub-clinical deficiencies occur extremely rarely, if they exist at all.

OBSERVATIONS CONCERNING THE INCREASE IN INTELLIGENCE SCORES IN CHILDREN

The pattern of observations 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 (Benton & Roberts, 1988; Benton & Buts, 1990; Benton & Cook, 1991*a*; Schoenthaler *et al.* 1991*a*,*b*). 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 (Cattell, 1943). If supplementation was to facilitate physiological functions then *a priori* it would be predicted that non-verbal scores would be influenced.

The consistency of the change in non-verbal intelligence makes it difficult to dismiss the findings. Anybody trying to explain away these findings has 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.

Benton (1991*b*) suggested that, in part at least, the apparent improvement in measures of non-verbal intelligence in response to supplementation may reflect improved attention. When intelligence tests are taken on a second occasion familiarity with the task often leads to an improvement in performance.

On four of the five occasions when improved intelligence scores have resulted from supplementation, the performance of those taking the placebo has either declined or not increased in the expected manner (Benton & Roberts, 1988; Benton & Buts, 1990; Benton & Cook, 1991*a*; Schoenthaler *et al.* 1991*a*). It is unlikely that the children would become less intelligent over a few weeks; a decrease in concentration or attitude would explain this profile.

Benton & Cook (1991*a*) 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, attentional problems cannot explain the findings entirely. Kerimova & Aleskerova (1990) examined a group of 120 6 year olds in Azerbaijan and found a vitamin supplement for 6 months 'significantly lowered fatigue . . . the working capacity and attention as well as nervous-reflectory activity were significantly improved . . .'. The Schoenthaler *et al.* (1991*b*) study is exceptional in the respect that the non-verbal intelligence of those taking the placebo 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. This absence of a poor performance when taking the placebo may reflect the use of individually administered tests in the Schoenthaler *et al.* (1991*b*) study, whereas other studies used either tests administered to groups or to young children, situations where the cooperation of the subjects would be harder to establish.

There is no suggestion that all children respond to supplementation. Benton & Buts (1990) used a dietary diary to identify one-third of the boys in a sample group whose diets supplied fewer micronutrients than the rest of the sample. This sub-group with the poor diet corresponded with those whose non-verbal intelligence was increased by the administration of supplements. The majority of these boys came from two of seven schools who took less-academically-able pupils from less-economically-advantaged areas. Schoenthaler *et al.* (1991*a*) found increases in non-verbal intelligence only in those whose levels of blood micronutrients increased following supplementation. Schoenthaler *et al.* (1991*b*) found that, although there was an overall average increase in non-verbal intelligence, there was a relatively large increase in 45% of the sample but only a limited response in the rest. Benton & Cook (1991*a*) found a greater response in children in a school in a more-socially-deprived area.

The weight of evidence suggests that not all children respond to supplementation; it does not suggest that all children whose diet supplies low levels of vitamins and minerals may benefit. Rather than saying that vitamins increase intelligence a more accurate statement would be that a poor diet may be associated with poor performance on non-verbal intelligence tests. The choice of child is critical, a particular school may or may not include a high percentage of children with dietary problems. The two studies that failed to find positive responses to supplementation (Crombie *et al.* 1990; Nelson *et al.* 1990) failed to distinguish well-fed from poorly fed children: the question they ask is whether all children respond; the answer no is non-controversial but it does not preclude the possibility that a minority will respond.

RESTRICTED DIETS AND PSYCHOLOGICAL SYMPTOMS

The idea that psychological measures may indicate the adequacy of diet is such an unusual suggestion that it is useful to marshal the arguments in its favour.

The feeding of diets lacking in particular micronutrients offers a means of establishing the initial symptoms that result from deficiency. Eating diets deficient in the B vitamins is associated with poor motor performance and changes in personality (Berryman *et al.* 1947). The first response to a thiamin-deficient diet is an inability to concentrate, confusion of thought, uncertainty of memory, anorexia, irritability and depression (Williams *et al.* 1942). Following deprivation the re-administration of thiamin produces dramatic changes, in particular appetite is rapidly restored and personality changes for the better (Brozek, 1957). Tuttle *et al.* (1949) found a low-thiamin diet to be associated with poor reaction times: an interesting conclusion of this study was that it is doubtful if a minimum thiamin requirement can be meaningfully established as there are wide individual needs. Sterner & Price (1973) found that a diet lacking riboflavin produced personality changes and poorer grip-strength, although perceptual measures and hand–eye coordination were not influenced. A diet low in ascorbic acid was associated with poor reaction times, severe fatigue (Farmer, 1944) and changes in personality (Kinsman & Hood, 1971).

Deprivation studies by their nature offer diets much lower in particular vitmins than are likely to occur naturally; thus, the findings should be interpreted with great care. The relevance in the present context is to support the point that, with some micronutrients at least, the first signs of deficiency are psychological in nature.

Although a deprivation diet will induce a deficiency at a fast rate, the possibility cannot be excluded that a poor diet, over an extended period, will so deplete the vitamin stores of particular individuals as to lead to sub-clinical deficiency symptoms. As an example, irritability, aggressive behaviour and personality changes have been described in adolescents suffering from thiamin deficiency arising from diets consisting largely of high-energy 'junk' foods (Lonsdale & Shamburger, 1980). Treatment with thiamin alone resulted in improvements in the symptoms, although previously they had failed to respond to drugs or psychotherapy.

THE ADEQUACY OF VITAMIN–MINERAL INTAKE IN INDUSTRIALIZED COUNTRIES

Using conventional biochemical definitions there is a consistent picture that the vitamin intakes of a minority of individuals are deficient or marginal (Sabry *et al.* 1974; Arab *et al.* 1982; Ehrhardt, 1986; Lemoine *et al.* 1986). Judging by these biochemical criteria, most of the population do not give cause for concern, but some individuals do.

The possibility exists that the incidence of marginal intake may be higher in sub-populations. Lopez *et al.* (1980) found a 26·6% incidence of riboflavin deficiency in a group of 210 New York adolescents from poor backgrounds. Lonsdale (1988) tested 1011 patients who approached a practice specializing in nutritional correction and found that 28%, were thiamin deficient. Carney *et al.* (1982) examined 172 successive admissions to a British psychiatric hospital and, based on biochemical assays for thiamin, riboflavin and pyridoxine, found that 53% were deficient in at least one vitamin. Malvy *et al.* (1989) assayed the serum of 392 healthy French schoolchildren for vitamins A and E and found 5% to be deficient in one or other of the vitamins.

The use of dietary diaries and the calculation of intake in terms of the recommended daily amount (RDA) is a second major way of assessing the adequacy of diet. Greenwood & Richardson (1979) reviewed the literature dealing with the diets of adolescents and concluded '. . . specific nutrient deficiencies have been identified in a significant proportion of the adolescent population. They include iron, calcium, vitamin A, vitamin C . . .'. We must look to the survey of *The Diets of British Schoolchildren* (Department of Health, 1989) as the most authoritative United Kingdom source on this topic. There was evidence of low intakes of Fe, Ca and riboflavin in teenage girls, and a generally low intake of pyridoxine. Where the average intake for particular nutrients reached accepted levels there were wide variations in individual consumption with evidence of a minority consuming 70% or even 50% of the RDA. We cannot conclude on the basis of these findings that anybody suffers from a sub-clinical deficiency but they strongly suggest that such a hypothesis should be taken seriously. Dietary surveys have produced little evidence inconsistent with the suggestion that there are sub-sections of the population who have a marginal intake of vitamins and minerals.

VITAMIN-MINERAL SUPPLEMENTATION AND IMPROVED FUNCTIONING

Given the multitude of functions served by vitamins and minerals in the central nervous system, it would be strange if a change in intelligence was the only manifestation of a sub-clinical deficiency. In fact if only intelligence changed when taking vitamin supplements this, in itself, would be an argument against the veracity of the finding.

It would be expected that during gestation and the early months of life, when the brain is growing rapidly, it would be easier to demonstrate whether or not a deficiency exists. The taking of folic acid by a mother in the early stages of pregnancy is associated with a decreased risk of neural tube defects (MRC Vitamin Study Research Group 1991). Harrell *et al.* (1956) found that the taking of vitamin supplements by mothers during the latter part of pregnancy was associated with higher intelligence scores at ages 3 and 4 years in one sample but not in another. They suggested that the response to supplementation reflected the poorer diet of the mothers whose children responded. Aukett *et al.* (1986) found that administration of Fe supplements was associated with increased weight gain and psychomotor development in infants aged 17–19 months.

Harrell (1946) gave thiamin supplements for 1 year to children whose diets, as judged by the RDA, supplied sufficient of this vitamin; they ended up taller, with quicker reaction times and scored better on tests of memory and intelligence than children taking a placebo. In normal members of the population selenium (Benton & Cook, 1991*b*) and multi-vitamin supplements (Heseker *et al.* 1990) have been found to improve mood. Dommisse (1991) marshals the evidence that cyanocobalamin deficiency is more widespread than is generally thought and, he argues, is responsible for a proportion of psychiatric disorders. There are reports of poor folic acid status being associated with depression (Coppen *et al.* 1986) and neurological problems (Reynolds *et al.* 1973). Botez *et al.* (1984) described a group of patients with low serum folic acid levels whose intelligence scores increased by over nine points following supplementation.

Nicotinamide supplementation has been reported to improve short-term memory (Loriaux *et al.* 1985). Supplementation with thiamin, pyridoxine and cyanocobalamin has been found to improve target shooting by marksmen (Bonke & Nickel, 1989). The intelligence scores of those with low blood ascorbic acid values have been found to increase when they consumed orange juice (Kubala & Katz, 1960).

Goodwin *et al.* (1983) related vitamin status to cognitive functioning in the elderly. Those with low levels of either ascorbic acid or cyanocobalamin scored badly on tests of abstract reasoning and memory. Smidt *et al.* (1991) studied a sample of randomly selected healthy elderly women and found that those receiving thiamin supplementation reported increased well-being and less fatigue. The administration of various micronutrients has been associated with improved mental health and other psychological measures in the elderly (Tolonen *et al.* 1985, 1988; Van Rhijn *et al.* 1990).

Without doubt the most extensively studied topic in this area is the influence of Fe deficiency on psychological functioning. Haas & Fairchild (1989) concluded that Fe therapy in children with Fe-deficiency anaemia has resulted in improvements in developmental progress, school performance, intelligence and other cognitive scores. Although the vast majority of these studies have been carried out in the Third World there are similar British findings (Aukett *et al.* 1986). Most studies have been carried out using children, although the short-term memory of pregnant mothers in the USA has been shown to improve in a double-blind study (Groner *et al.* 1986).

DISCUSSION

The proposition that vitamin–mineral supplementation may enhance psychological functioning readily attracts criticism. Yet a series of papers in mainstream medical and scientific journals have been described that report a wide range of psychological responses to supplements of vitamins and minerals; most are well-designed double-blind placebo-controlled studies, although some are clinical reports or correlational in nature. As would be predicted a range of factors are influenced including mood, personality, cognitive measures including intelligence scores and memory.

Psychological measures have been used infrequently to study the adequacy of diet, although when subjects are experimentally deprived of vitamins, psychological changes are often amongst the first to be observed. 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. Psychological measures may prove to be a sensitive means of demonstrating sub-clinical deficiencies of micronutrients as they are a reflection of the integrated functioning of the nervous system.

The available evidence is such that the hypothesis that sub-clinical deficiencies of micronutrients disrupt psychological functioning should be taken seriously. First, in virtually all studies of the adequacy of diet there is a minority whose intake of micronutrients is below that considered optimal. Second, there is a growing list of well-designed studies, in both children and adults, that report a positive response to supplementation. The full nature, extent and implications of the existence of sub-clinical vitamin deficiences are topics that await a great deal of research.

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