Alzheimer's Disease: The Nutritional Hypothesis

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Abstract

The author reviews the arguments for the nutritional etiology (malnutrition with or without digestive malabsorption) in Alzheimer's disease (AD). They have been grouped in four parts:
1) AD is associated with malnutrition, and probably with digestive malabsorption.
2) Many data suggest that A D is the consequence and not the cause of malnutrition: chronic deficiency in calcium and magnesium is probably the cause of Guam parkinsonism-dementia complex which is characterized by two of the three main neuropathologic changes of AD, and neurofibrillary changes have been described as the consequence of severe malnutrition, etc.
3) Down's syndrome (DS) and AD. All the patients with DS develop at or slightly before their fourth decade, the neuropathologic changes of AD. A review of the literature and personal observations show they suffer from malnutrition, probably owing to malabsorption.
4) Explanatory interest of the nutritional hypothesis. This hypothesis might explain many of the clinical, anatomical, neurobio-chemical, etc. data described in AD.

Introduction

The cause(s) of Alzheimer's disease (AD) is unknown. Recently, the following have been proposed as possible causes: a slow virus; a prion (special infective protein particle); aluminium; auto-immune reactions against the brain; a genetic disorder; and malnutrition with or without malabsorption.

In this paper, the arguments for the nutritional hypothesis will be reviewed. They have been divided in four parts.
I) AD is associated with malnutrition.
II) Many data suggest that AD is the con
sequence and not the cause of malnutrition.
III) AD and Down's syndrome (DS).
IV) Explanatory interest of the nutritional hypothesis.

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I) AD is associated with malnutrition. Mainutrition could be the consequence of digestive malabsorption.

Many data show that patients with AD suffer from malnutrition (1). These are the following:
— cachexia and emaciation, which are quasi-constant, particularly at the end of the disease (1, 2, 3, 4);
— the high frequency of infections, particularly pulmonary and urinary tract infections (1,5,6);
— low blood levels of vitamins B2, B6, C (7,8,9), B_{12} (10, 11, 12, 13, 14), and of folic acid (9,11,15), prealbumin (8), glucose (16), iron (17), tryptophan (9) and hemoglobin (5).

It is important to notice that normal weight or obesity do not exclude malnutrition: oedema and/or prior obesity and/or slow mobilisation of fat can obscure tissue loss. It is also important to notice that blood nutritional analytes in the normal range do not exclude malnutrition: subclinical or clinical dehydration may obscure abnormally low blood nutritional analytes such as hemoglobin (18).

Malnutrition in AD could be the consequence of digestive malabsorption. In fact, data suggest malabsorption in AD: e.g. the association of hyperphagia with a malnutrition syndrome, and with cachexia (1); low body weight despite high energy intake (1); and the description of tryptophan malabsorption (19). It is important to notice that the absence of diarrhea, or even the presence of constipation, does not preclude a malabsorption syndrome and that malabsorption could be the consequence as well as the cause of malnutrition (1). It has been suggested (1) that malabsorption could be more frequent in presenile cases than in senile ones.

II) Many data suggest that AD is the consequence and not the cause of malnutrition:

— the parkinsonism-dementia complex on Guam Island, which is characterized neuro-

pathologically by two (neurofibrillary degeneration and granulovacuolar degeneration) of the three main cerebral lesions of AD (2) (the third being the senile plaque) is probably caused by chronic nutritional deficiency in calcium and magnesium (20, 21, 22). This is due to the poverty of these two minerals in the soil, to the preference for traditional food (20, 21, 22) and to a lower subsistence level (22);

— neurofibrillary degeneration is the consequence of malnutrition (review of the literature prior to 1925 by Jackson) (23) and of cholera, intestinal tuberculosis and bacillary dysentery (24); (Alexander's observations suggest that the amyloid core of the senile plaque could be the nucleus of a degenerated cell);

— the number of senile plaques could increase with the fall of the serum iron level (17);

— Skullerud (25) has shown that in women, the quantity of Alzheimer's neurofibrillary changes increases with decreasing body mass index;

— the number of the cases of senile dementia increased in a context of severe underfeeding (26);

— dementia and organic psychosyndrome with brain atrophy have been described in concentration-camp survivors and ex-Far-East prisoners of war (27, 28, 29, 30, 31). They are the consequence of severe underfeeding during the war (27,28) and are possibly also the consequence of the persistence of a state of malnutrition after the war (28). Niacin could be beneficial to ex-Far-East prisoners of war (32);

— malabsorption syndromes can induce dementia (33);

— intellectual deterioration is a consequence of underfeeding (26, 34, 35);

— in the elderly, poor performance on cognitive tests is associated with low intake and serum levels of riboflavin, folate, vitamin B_{12} and ascorbate (36).

III) Down's Syndrome (DS) and AD

All the subjects with DS develop the neuropathologic changes of A D at or slightly before their fourth decade (2, 37). This hypothesis implies that they suffer from malnutrition with or without malabsorption.

A review of the literature and personal observations (1) show that these patients suffer from malnutrition:

— Clinically, they show signs of vitamin deficiencies (1, 38);

— They have low or deficient blood values for vitamin B_1, nicotinic acid and ascorbic acid (39, 40, 41);

— Their red cell folate values are in deficient (42);

— They present the immunological signs of malnutrition (6): unusual susceptibility to infection (43, 44), impaired neutrophil bactericidal capacity (45), depressed reactivity to skin-test antigens (46), decreased responsiveness of lymphocytes to mitogens (43,47, 48), decreased capacity of peripheral blood lymphocytes to form rosettes with sheep red blood cells (43, 47).

Furthermore, an association has been shown in DS between intellectual deterioration and macrocytosis (49), which is mainly nutritional in origin and which is correlated with the decrease in the serum folic acid level (42).

Many data suggest malabsorption in DS: deficient or low blood values for vitamin B_1, nicotinic acid and ascorbic acid despite adequate dietary intake and ascorbic acid and vitamin B_1 supplements (39, 40, 41), impaired digestive absorption of vitamin A (50, 51), and xylose excretion below normal after oral administration of a xylose load (52).

IV) Explanatory Interest of the Nutritional Hypothesis

The nutritional hypothesis could explain many of the data of Alzheimer's disease.

Clinical data Malnutrition with or without malabsorption may explain neurological signs (absence of one or more deep tendon reflexes, ataxia, paratonic rigidity — "gegen-halten" —, etc.) and psychiatric signs (disorders of memory and of judgement, disorientation, delusions, depression, delirium, etc.) described in the disease. The predominant lack of one or more nutrients could explain the predominance of certain symptoms in a patient (1). This hypothesis could explain the aggravation or the appearance of the disease when the patient receives a trauma, develops an infection, undergoes surgery or encephalography, or is hospitalized: these circumstances are often accompanied by a feeding deficiency which, in turn, aggravates malnutrition (1). Brain

lesions or neurochemical disorders have been proposed to explain terminal cachexia with or without hyperphagia in AD: malnutrition with or without malabsorption could also explain it (1).

Brain metabolism Low cerebral metabolism of glucose and oxygen could be explained by malnutrition (1).

Anatomical data Ventricular dilation in AD (53) which correlates with the rate of neuro-psychological deterioration (54) can be explained by malnutrition (25). Deficiencies in protein, vitamin E, selenium, sulphur-containing amino-acids, chromium, and poly-unsaturated fatty acid could explain neuronal lipofuscin accumulation (55).

Brain biochemistry disorders In the brain of patients with AD, losses of choline acetyl transferase, acetylcholine esterase, noradrenaline, dopamine B hydroxylase, dopamine and homovanilic acid and reduced acetylcholine synthesis have been described (56). Such perturbations could be explained (1) by deficiencies in nutrients which are necessary for the synthesis or the activity of these molecules: essential amino-acids, vitamins (particularly vitamin B_5 — co-enzyme A —which forms acetylcholine with choline, etc.), minerals, trace-elements, etc. (1). Such perturbations could also be explained by neuronal loss due to malnutrition, which is a cause of neuronal loss (24).

Brain aluminium accumulation Malnutrition could also explain the accumulation of aluminium in the brain of patients with AD: it causes an accumulation of aluminium in the rat brain (57).

Therapeutic data This hypothesis explains the lack of success of treatments by the precursors of the neurotransmitters (choline, tryptophan, or tyrosine). There is no point in feeding with precursors if the enzymes cannot metabolize them because of their deficiencies in co-factors (vitamins, minerals, trace elements) (1).

Genetic data Very rare familial cases of AD would seem to be genetic in origin: these forms could be explained by the genetic character of certain forms of malabsorption (1).

Discussion

The signs of malnutrition described in AD and DS are signs of protein-calorie malnutrition and of protein malnutrition. Studies are necessary to determine to which nutrient(s) such and such a brain lesion or neuchemical disorder could correspond.

Guam studies (21, 22) and the appearance in early life of nutritional deficiencies in patients with DS suggest that AD is the consequence of very long-term malnutrition. The consequences of malnutrition concern the whole body: for us, AD is a disease of the whole body and not only a disease of the brain. This hypothesis does not exclude psychogenic or sociogenic causes for AD: malnutrition might be the consequence of depression or loneliness in the elderly (1). Even if the hypothesis that malnutrition is the consequence of the mental state of patients with AD cannot be excluded, further studies are obviously needed.

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Introducing The Around The World Column

Early in 1987, Dr. Gert E. Schuitemaker, Editor of *Orthomoleculair,* began to write to me. Dr. Schuitemaker has been interested in Orthomolecular medicine for six years and had been promoting it in Europe by editing a journal, giving courses and organizing seminars.

According to Dr. Schuitemaker, Orthomolecular medicine in Europe lags behind England. In Europe, government laws and restrictions regarding supplements have held back interest. In the Netherlands, it is possible to distribute supplements freely but the government is threatening to impose restrictions. In Belgium there is no problem. The laws in Scandinavian countries, Germany, Switzerland and France make it impossible to distribute vitamins as foodstuff.

Dr. Schuitemaker suggested that we collaborate in disseminating information by having an *Around the World* column in several Orthomolecular journals. Three of us have agreed this is an excellent idea. Beginning in 1988 this will be a regular feature of *The Journal of Orthomolecular Medicine,* of *Orthomoleculair,* and of *International Clinical Nutrition Review.*

The three editors will be responsible for preparing material which will be sent to Dr. Schuitemaker, who will be the International Editor of *Around the World.* The editors are:

1. Dr. A. Hoffer, 3A - 2727 Quadra Street, Vancouver, British Columbia, Canada V8T 4E5;
2. R. A. Buist, Ph.D., Editorial Office, International Clinical Nutrition Review, P.O. Box 370, Manly, New South Wales 2095, Australia;
3. D.rG. E. Schuitemaker, European Institute for Orthomolecular Science, Postbus 420, 3740 AK Baarn, The Netherlands.

Contributions are solicited from scientists.

In this way, we can keep ourselves informed about developments in Europe, Australia and the U.S.A. and Canada.

A. Hoffer, M.D., Ph.D.