

Low Levels of Triiodothyronine in Patients with Alzheimer's Disease

Dear Editor,

There is substantial degree of disagreement regarding the mechanisms of possible association between thyroid dysfunction and Alzheimer's disease. For example, it is not settled which indicator of thyroid function is the best marker of this relationship. Since thyroid disorders could be considered as treatable risk factors for Alzheimer's disease, identification of any relationship between them would be of great value. Recent investigations have provided further evidence that not only overt thyroid disorders but also subclinical changes in thyroid function and even thyroid hormone variations within the normal range can influence cognitive performance.¹⁻³

In order to examine possible relationship between thyroid function and Alzheimer's disease, we did compare serum levels of total thyroxine (T4), total triiodothyronine (T3), T3 resin-uptake (T3Ru) and thyroid stimulating hormone (TSH) levels of 51 patients with Alzheimer's disease, aged 55 years or older, with those of 49 healthy volunteers of similar age who met our exclusion criteria and served as control group. The diagnosis of Alzheimer's disease was performed using Diagnostic and Statistical Manual of Mental disorders, 4th ed (DSM-IV) criteria. Venous blood samples were taken for the measurement of serum total T4, total T3 resin uptake (T3Ru) and TSH levels by radioimmunoassay method. Independent t-test was used to compare mean values of age, BMI, and thyroid function indices. The data were analyzed using Statistical Package for Social Sciences (SPSS, version 9). A P value of ≤ 0.05 was considered statistically significant.

There were no relations between age, sex or body mass index (BMI) and thyroid function. Although, the mean serum levels of T4, TSH and T3Ru from patients with Alzheimer's disease were not statistically different from those of the controls, the patients had significantly lower serum levels of T3 ($P=0.03$).

Five patients and five controls had subclinical hypothyroidism ($TSH>4.5$). Moreover, six control subjects and none of the patients had subclinical hyperthyroidism ($TSH<0.3$). However, the sample size was not enough to detect significant difference between them.

The serum levels of T3 was lower in patients with Alzheimer's disease indicating that there might be an association between serum levels of T3 and the disease. Such a conclusion receives support from a previous study by Gussekloo and colleagues, who showed that in an unselected general population of 558 individuals aged 85 years low free T3, but not TSH or T4, were associated with an accelerated decline in global cognitive function.⁴ There are well-documented observations that thyroid hormones control apoptosis in the brain.^{5,6} Moreover, *in vivo* and *in vitro* studies have demonstrated the inhibitory effect of T3 in the regulation of amyloid-beta protein precursor secretion as a major component of Alzheimer plaques in the brain.^{2,7,8} The lower levels of T3 in the patients in the present study may be due to co-morbid conditions associated with aging process. However, we did try to keep our results free of co-morbidity as much as possible by excluding patients who had acute debilitating illnesses, and all of our patients were ambulatory.

In conclusion, the present study suggests that a reduced level of T3, within the normal range, may be independently associated with cognitive decline in Alzheimer patients.

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