Role of thyroid hormones in the effects of selenium on mood, behavior, and cognitive function

L. Sher
Riverdale, New York, USA

Summary Changes in thyroid function may affect mood, behavior, and cognitive function. Selenium is required for appropriate thyroid hormone synthesis, activation, and metabolism. Selenium status influences thyroid function. Selenium status also affects psychological condition and cognitive function. The author suggests that the effects of selenium status on mood, behavior, and cognition may be partly mediated by changes induced by selenium deficiency or selenium supplementation in thyroid function. Selenium deficiency decreases immunocompetence and promotes viral infections. The author proposes that patients who have a combination of depression, hypothyroidism, and increased susceptibility to viral infections, could reasonably be assessed for selenium deficiency, especially if they live in an area where the soil is low in selenium.

EFFECTS OF THYROID HORMONES ON MOOD, BEHAVIOR, AND COGNITIVE FUNCTION

It has been well known for many years that both hypo- and hyperthyroidism may cause various psychiatric symptoms (1,2). Both hypo- and hyperthyroidism may be associated with changes in mood, behavior, and cognitive function. Considerable evidence has accrued within the last several decades indicating that the boundary between normal thyroid function and thyroid dysfunction is not distinct.

There is substantial evidence that small changes in thyroid function might be biologically meaningful and affect mood and behavior (1–4). We studied blood levels of free thyroxine (T4) and thyroid-stimulating hormone (TSH) in patients with seasonal affective disorder (SAD) and matched controls in the winter (3). We found that free T4 blood levels were slightly but significantly lower in patients than in healthy volunteers. The difference between TSH levels in SAD patients and controls was not statistically significant. All patients with SAD were required to be physically healthy on physical examination and routine laboratory testing, i.e., abnormal thyroid values would have excluded patients from the study. Our findings might thus have been attenuated as a result of our screening practices. The results of our study support the opinion that even the small difference between patients and controls could be biologically meaningful (5–9).

In subclinical hypothyroidism thyroid hormone concentrations fall within the normal range (1,4). Subclinical hypothyroidism is a relatively common disorder with an overall prevalence of 5–10% (10,11). By definition, subclinical hypothyroidism does not produce the features of clinical hypothyroidism. However, dry skin, cold intolerance, fatigue, alterations in lipid metabolism and cardiac function, lower scores on memory tests, and higher scores on ratings of anxiety have been observed in subclinical hypothyroidism (1,2,4,12).

The brain utilizes thyroid hormones differently than do other organ systems (4,13). Despite the fact that the brain has a unique ability to locally control the conversion of T4 to T3, the brain may be especially sensitive to mild thyroid...
insufficiency. Esposito and colleagues (14) reported a 75% lifetime prevalence of major depression in patients older than 64 years with subclinical hypothyroidism compared with an 18% prevalence in matched euthyroid controls. Haggerty and colleagues (15) reported a 56% lifetime prevalence of major depression in non-elderly women with subclinical hypothyroidism, compared with 20% in euthyroid women. Similar findings have been described in other studies (2,4,16). It has been suggested that even subtle decrement in thyroid system resiliency may impair recovery from depression (4,12).

Cognitive associations of clinical hypo- and hyper-thyroidism are well known (1). However, even subtle changes in thyroid function may affect cognition. Prinz et al. (17) reported that pooled 24-hour samples of thyroid hormones have significant positive associations with measures of overall cognition, even when hormones are within normal ranges, and in the absence of overt physical or mental illness.

EFFECTS OF SELENIUM ON THYROID FUNCTION

The element selenium, named after the Greek goddess of the moon Selen, was discovered by the Swedish scientist Berzelius in 1817 (18,19). Selenium is an essential nutrient of fundamental importance to human biology (18–21). Selenium in blood is taken up by erythrocytes (50–70% within 1 min) and is distributed to the tissues via selenium binding proteins (20). The half-life of selenium in the human body is approximately 65–115 days.

Selenium is required for appropriate thyroid hormone synthesis, activation, and metabolism (19–22). The human thyroid gland has the highest selenium content per gram of tissue among all organs. Several selenocysteine-containing enzymes are functionally expressed in the thyroid: three forms of glutathione peroxidases, the type I 5-deiodinase, thioredoxin reductase and selenoprotein P. Selenoproteins control thyroid hormone metabolism in non-thyroidal tissues where the prohormone T4 is converted to biologically active T3 or its inactive isomer rT3 (22).

Deiodinase activity is relatively protected in conditions of marginal selenium availability (21,22). However, low levels of selenium intake may compromise thyroid-hormone metabolism. In an animal model, a 47% reduction in the activity of the type I 5-deiodinase enzyme has been reported secondary to selenium deficiency (23). Olivieri et al. (24) reported that selenium supplementation in a group of elderly individuals decreased plasma thyroxine concentrations, consistent with increased deiodinase activity and improved conversion to the active hormone, T3.

A combination of selenium and iodine deficiency exacerbates hypothyroidism and may manifest itself as myxedematous cretinism, such as seen in the areas where deficiencies in both these minerals exist (19,20,22). The development of myxedematous cretinism may be related to oxidative damage induced by exaggerated thyrotropin dependent hydroxide peroxide production in the thyroid (20). Selenium status may be a major determinant of the outcome of iodine deficiency in both humans and animals.

EFFECTS OF SELENIUM ON MOOD, BEHAVIOR, AND COGNITIVE FUNCTION

Multiple lines of evidence suggest that selenium deprivation leads to depressed mood, and high dietary or supplementary selenium seems to improve mood (21,25–27). Several research groups found that low selenium status was associated with a significantly increased incidence of depression, anxiety, confusion, and hostility. Low plasma selenium concentrations in the elderly were significantly associated with senility and cognitive decline (28). It has also been reported that brain selenium level in Alzheimer’s patients was only 60% of that in controls (21).

Hawkes and Hornbostel (25) studied effects of dietary selenium on mood in healthy men as assessed by the Profile of Mood States-Bipolar Form. Eleven healthy men were confined in a metabolic research unit for 120 days. The diet of conventional foods provided 80 micrograms/day of selenium for the first 21 days, then either 13 or 356 micrograms/day for the remaining 99 days. There were no significant changes in any of the mood scales due to dietary selenium. However, in the low-selenium group, the changes in the agreeable-hostile and the elated-depressed subscales were correlated with initial erythrocyte selenium concentration; that is, the lower the initial selenium status, the more the mood scores decreased.

Finley and Penland (26) also studied effects of dietary selenium on healthy men who were fed either a low or a high selenium diet for 15 weeks. Individuals on the low selenium diet had significantly decreased clearheaded/confused and elated/depressed subscores, those on the high selenium diet significantly improved in the clear-headed/confused, confident/unsure, and composed/anxious subscores.

Benton and Cook (27) examined the possibility that a subclinical deficiency of the trace element selenium might exist in a sample of the British population. A selenium supplement was given for 5 weeks. Using a double-blind cross-over design, 50 subjects received either a placebo or 100 micrograms of selenium on a daily basis. On three occasions they filled in the Profile of Moods States. Selenium intake was associated with a general elevation of mood and in particular, a decrease in anxiety. The change in mood when taking the active tablet was correlated with the level of selenium in the diet, which was estimated...
from a food frequency questionnaire. The lower the level of selenium in the diet the more reports of anxiety, depression, and tiredness, decreased following 5 weeks of selenium therapy.

**DISCUSSION**

Changes in thyroid function may significantly affect mood, behavior, and cognitive function. Selenium status influences thyroid function. Selenium status also affects psychological condition and cognitive function of healthy and sick persons. The effect of selenium status on mood, behavior, and cognition may, therefore, be partly mediated by changes induced by selenium deficiency or selenium supplementation in thyroid function (29).

Selenium deficiency decreases immunocompetence and promotes viral infections (21,30,31). In a selenium-deficient host harmless viruses can become virulent (31). Patients who have a combination of depression, hypothyroidism, and increased susceptibility to viral infections, could reasonably, therefore, be assessed for selenium deficiency, especially if they live in an area where the soil is low in selenium.

The study of the effects of selenium status on psychological well being is still in its infancy. Many methodological problems warrant consideration in studies of diet-behavior relationships (32). These include questions regarding research design, effect sizes, the timing of nutrient-related changes, individual differences, etc. The potential background influences of circadian rhythms, the intake of multiple nutrients, dietary habits, and other factors should be unraveled.

Selenium and iodine were washed out from the upper layers of the soil during and after the ice ages in many regions of the world (19). Adequate supply with these essential compounds can be provided either by a balanced diet or supplementation. Iodine prophylaxis had been initiated during the 1920s (19). Future studies may answer the question of whether in addition to iodine prophylaxis we will also need selenium supplementation in order to optimize the function of the thyroid hormone axis in healthy and sick people.

**REFERENCES**


