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Cognitive Performance and Mood Changes in the Post-thyroidectomy Patient Treated with T4 versus T4+T3

Lorena Likaj, MPH

Abstract

This study investigated changes in cognition and mood in the post-thyroidectomy patient. Specifically, this study investigates changes in cognition and mood, when the patient has been returned to normal, laboratory serum thyroid-stimulating hormone (TSH) reference levels, following conventional thyroid hormone replacement therapies with levothyroxine (T4) alone. Findings reveal a distinct, small, and clinically significant subgroup of post-thyroidectomy patients (10–15%) who continue to experience impaired cognition and mood, even when routinely measured serum TSH levels have been returned to normal levels. Findings are discussed within a conceptual matrix emphasizing the differential role of deiodinase enzymes required for conversion of T4 to T3 within the brain (Type II), compared to T4 to T3 conversion completed in peripheral tissues.

Problem

Many patients with hypothyroidism, induced by a complete thyroidectomy, develop depression, decrease in cognitive function, and other psychiatric symptoms. These symptoms are reversed with thyroxine (T4) replacement therapy.

In these patients, the standard of treatment is daily administration of levothyroxine, a synthetic form of thyroxine (T4). The administration of T4 replaces the low levels of T4 resulting from the surgical destruction of the thyroid gland. The administered T4 is then converted to T3 peripherally and in the brain through the usual processes.

Of interest to us is the fact that, despite treatment and achievement of euthyroid levels as measured by routine plasma levels, 10-15 % of patients continue to experience a decrease in cognitive function and depression despite normal serum concentration of T4 and T3.

Purpose

The purpose of this study is to investigate changes in mood and cognitive function in post thyroidectomy patients. The reason this study is important is because there are few studies that investigate treatment of hypothyroidism in the post thyroidectomy patient.

Relevant Literature

Authors	Year	Journal	Title
Wiersinga	2014	Nature Reviews Endocrinology 10, 164-174.	Paradigm shifts in thyroid hormone replacement therapies for hypothyroidism
Biondi and Wartofsky	2012	Journal of Clinical Endocrinology & Metabolism 97 (7), 2256-2271.	Combination treatment with T4 and T3. Towards personalized replacement therapy in hypothyroidism
Panicker, Saravanan, Vaidya, Evans, et. al.	2009	Journal of Clinical Endocrinology & Metabolism 97 (7),.	Common variation in DIO2 gene predicts baseline psychological well-being and response to combination thyroxine plus triiodothyronine therapy in hypothyroid patients.
Kim and Bianco	2009	Journal of Clinical Endocrinology & Metabolism 94, 1521-1523.	For some, L-thyroxine replacement might not be enough: A genetic rationale.
Torlonano, Durante, Torrente, et al.	2008	Journal of Clinical Endocrinology & Metabolism 93, 910-913.	Deiodinase type II polymorphism (threonine 92 alanine) predicts L-thyroxine dose to achieve target thyrotropin levels in thyroidectomy patients.

Procedures

A systematic review of the professional medical literature was used to summarize existing knowledge, test specific research questions, and evaluate the proposed model.

Seven studies, meeting specific inclusion and exclusion criteria, were selected as representative of all studies identified by the systematic review and are presented here.

Limitations

This investigation is a systematic review of the literature and limited only by the constraints of the research design.

Conclusions

The use of T4 in combination with T3, in restoring post-thyroidectomy patients to an euthyroid state, is controversial among clinicians. Data from this review reveal :

- 10-15% of post-thyroidectomy patients evidence impairment in cognition and mood, despite serum TSH levels being returned to normal reference value levels on T4 therapy alone.
- Treatment with T4+T3 generates more favorable results than treatment with T4 alone.
- Data support the proposed model of down regulation of deiodinase enzyme type II in brain, as casual in explaining differences

Research Questions

- Do post-thyroidectomy patients, who have been returned to normal thyroid stimulating hormone levels, by way of conventional hormone replacement therapies, continue to experience impairments in cognition and mood?
- Can differences in the post-thyroidectomy patients, who continue to experience impaired cognition and mood, be explained by the hormone replacement therapy intervention, T4 alone versus T4 in combination with T3?
- Does review, summary, and critical analysis of the professional medical literature, from the period 1985- 2015, support a proposed new model, emphasizing down regulation of deiodinase enzymes type II in brain, as potentially causal in explaining differences between post-thyroidectomy patient who's cognition and mood improves with conventional hormone replacement therapies (80-85%) and post-thyroidectomy patients, who fail to demonstrate significant improvements in cognition and mood?

Findings

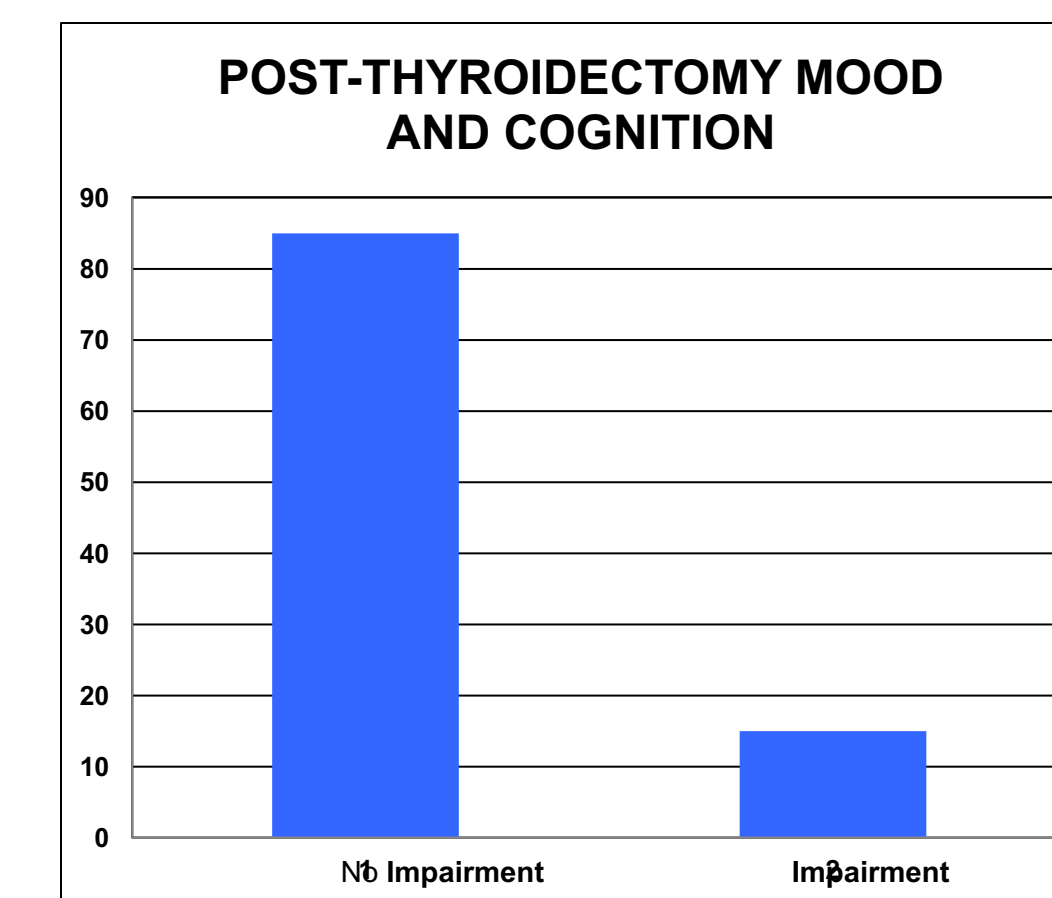


Figure 1. Percentage of patients evidencing no impairment and impaired cognition or mood, following thyroidectomy, when serum thyroid values have been returned to normal reference values. N = 397. Not impaired = 85%, Impaired = 15%, p < 0.05. Original data extracted and reanalyzed from Bianco, A. and Casula, S. (2012).¹¹

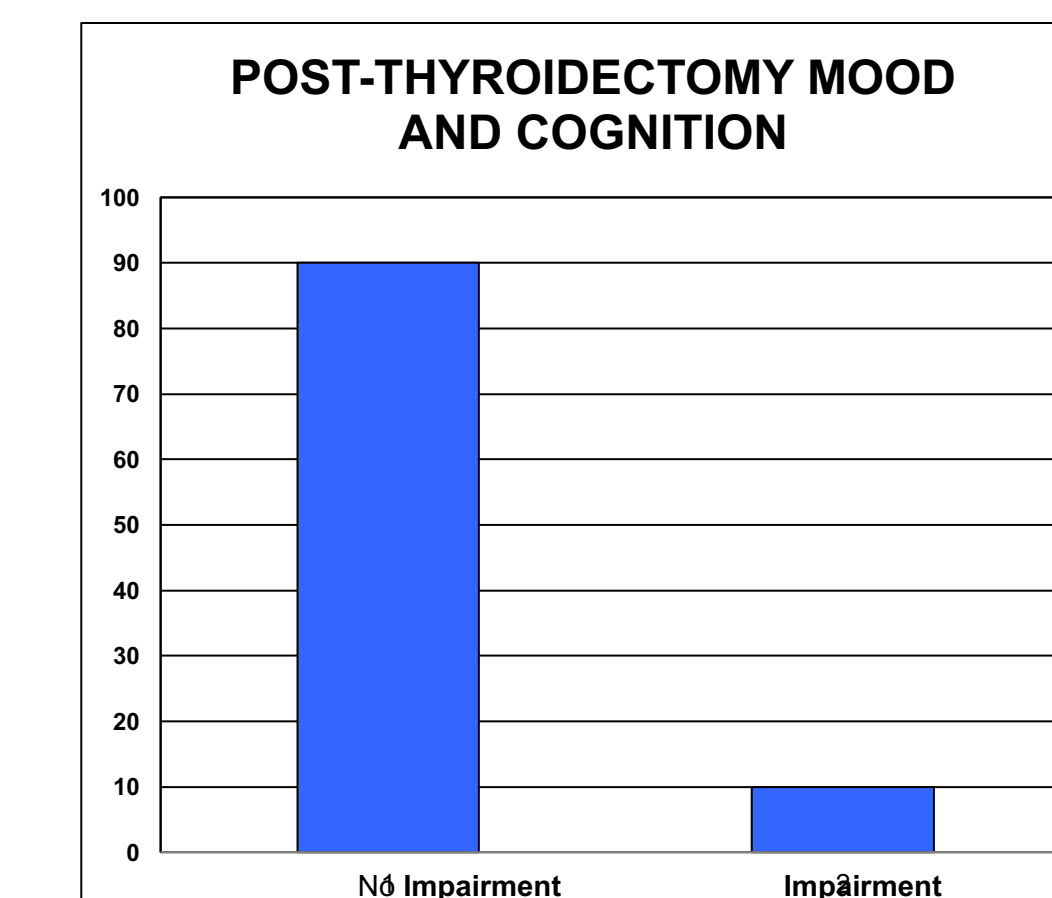


Figure 2. Percentage of patients evidencing no impairment and impaired cognition and mood, thyroidectomy, when serum thyroid values have been returned to normal reference values. Not impaired = 90%, Impaired = 10%, p < 0.05. Original data extracted and reanalyzed from Wiersinga (2014).¹²

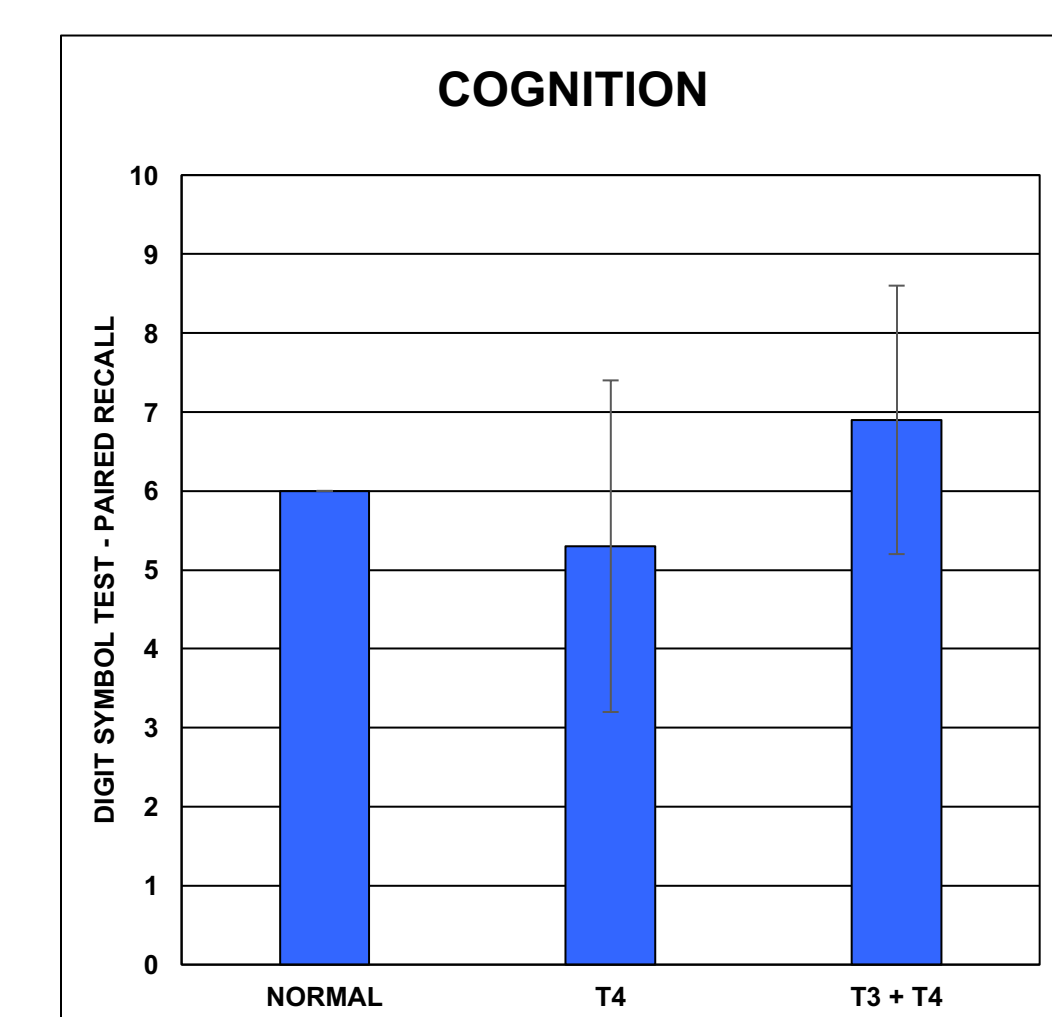


Figure 3. Correctly matched number and symbol - paired recall. Normal performance is 5 or more, with a maximum possible score of 9. N = 15 women patients with hypothyroidism, treated originally with T4 alone, and then treated with T4 + T3. Original data extracted and reanalyzed from Bunevicius and Prange (2000).¹⁴ Paired t-test T4 with T4+T3, p < 0.02.

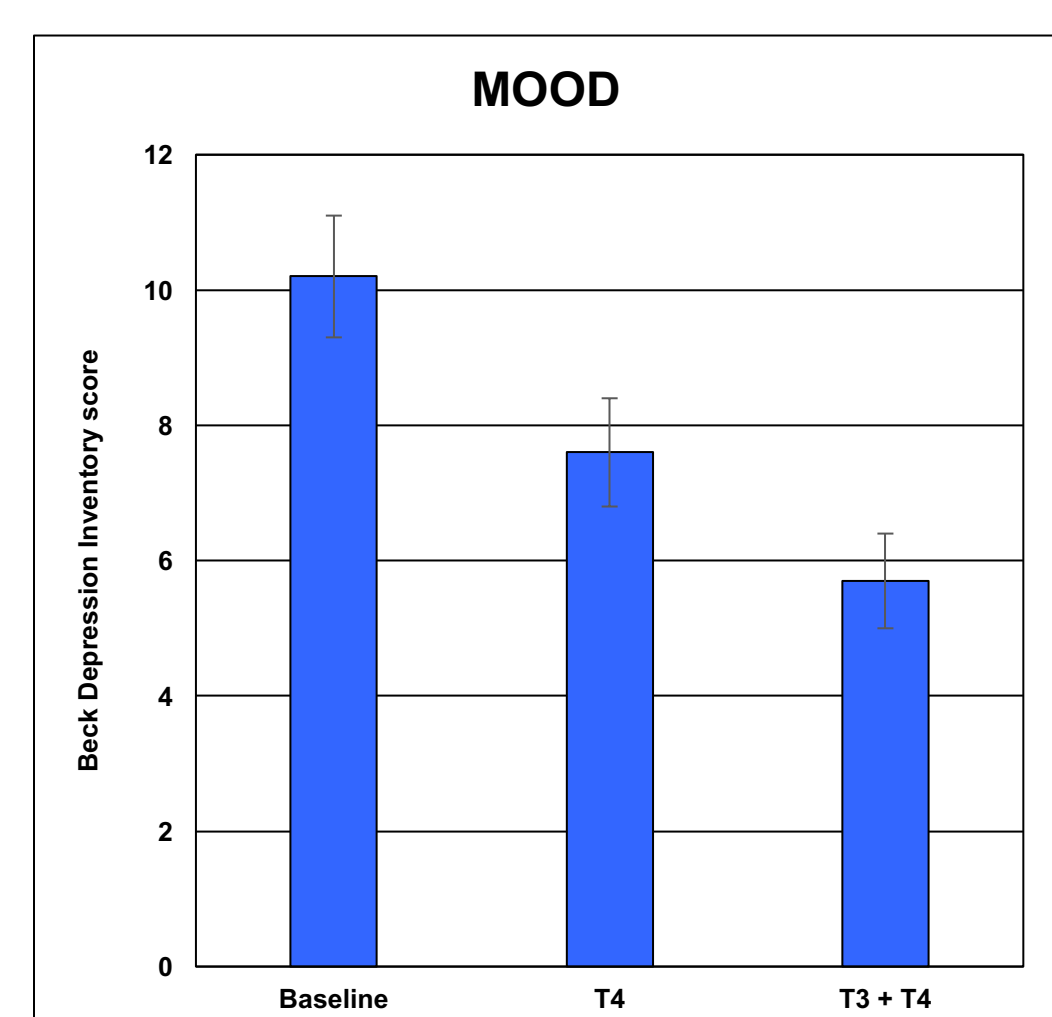


Figure 4. Beck Depression Inventory scores greater than 10 are associated with impaired and depressed mood. N = 59 patients with autoimmune hypothyroidism on stable T4 treatment times six months, and then treated with T4+T3. Randomized, double blind, cross-over, experimental research design. Original data extracted and reanalyzed from Nygaard, Jensen, Kvetny, et. al. (2009).¹⁵ Paired t-test T4 with T4 + T3, p < 0.01.

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