

Thyroid Disease and Cognition

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KEYWORDS

- Hypothyroidism • Thyrotoxicosis • Subclinical hypothyroidism
- Subclinical thyrotoxicosis • Mood • Cognition

KEY POINTS

- Alterations in mood and cognitive function are common in overt hypothyroidism and usually improve with therapy. These alterations can include anxiety, depression, and widespread cognitive decrements, particularly in memory functions.
- Alterations in mood and cognitive function are common in overt thyrotoxicosis and usually improve with therapy. These alterations can include anxiety and depression, and cognitive decrements in attention, concentration, and executive function.
- Subtle alterations in mood and cognitive function may exist in subclinical hypothyroidism and subclinical thyrotoxicosis, but major decrements are not seen. Cognitive deficits are primarily in working memory and executive function.

INTRODUCTION

The occurrence of psychological and cognitive changes in adults with altered thyroid function has been known for many years. In the late nineteenth century, reports first described hypothyroid and thyrotoxic patients with a range of mental disturbances.^{1,2} In modern times, earlier diagnosis of thyroid disorders has reduced the incidence of severe clinical disease, but patients still occasionally present with profound mental and behavioral changes.

Advances in neuroscience have led to validated neurocognitive tests that measure specific cognitive domains, mapped to critical brain regions. These advances allow for sensitive and targeted investigations of cognitive function, which reveal the presence of subtle affective and cognitive disturbances in hypothyroidism and thyrotoxicosis. The purpose of this review is to synthesize current data on central nervous system dysfunction in altered thyroid states and to provide clinical recommendations based on these data. Only adult-onset disease will be considered, as effects of congenital and childhood onset thyroid dysfunction are beyond the scope of this review.

There are 4 categories of thyroid dysfunction considered here, based on laboratory testing of free thyroxine (fT4), triiodothyronine (T3), and thyroid stimulating hormone

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(TSH) levels. Overt hypothyroidism is defined as a low-serum fT4 and elevated TSH level, whereas overt thyrotoxicosis is defined as a high-serum fT4 and/or T3 and suppressed TSH level. More subtle degrees of altered thyroid status include subclinical hypothyroidism (elevated TSH, normal fT4) and subclinical thyrotoxicosis (suppressed TSH, normal fT4 and T3). Although these entities are discussed separately, in reality they represent a continuum of thyroid function and dysfunction.

It is important to include affective disorders in a discussion of cognitive effects of altered thyroid status because thyroid dysfunction can directly alter mood, and mood decrements, in turn, can impair cognition. Therefore, effects of thyroid dysfunction on mood will also be considered in each section.

Before discussing specific types of thyroid dysfunction, it is helpful to emphasize issues that pertain to the entire field. The literature can be divided into larger cross-sectional or longitudinal studies and smaller interventional studies. Many older studies of either type were limited by small sample sizes, heterogeneous subject groups, or cognitive tests of limited sensitivity. For these reasons, much of the literature is inconclusive or inconsistent. More recent influential studies have been larger and/or have used more modern cognitive tests. This review briefly summarizes the older literature and emphasizes in more detail recent studies that have advanced the field. **Table 1** provides a broad summary of mood and cognitive alterations in the 4 types of thyroid dysfunction considered herein.

Thyroid Condition	Effects on Mood	Effects on Cognitive Function
Overt hypothyroidism	Likely increased rates of anxiety, depression Largely reversible with L-T4 treatment Rarely, "myxedema madness"	Widespread mild to moderate decrements, especially in memory Largely reversible with L-T4 treatment
Subclinical hypothyroidism	Mild symptoms of depression or anxiety may be present, not reliably improved with L-T4 treatment Some symptoms may be related to self-knowledge of thyroid disease Moderate to severe mood alterations not typical	Mild defects in memory, executive function Reverse with L-T4 treatment Major cognitive deficits not seen
Overt thyrotoxicosis	Symptoms of irritability, agitation are common May have increased rates of depression or anxiety Affective symptoms usually improve with β -blockers or definitive therapy Rarely, "thyroid storm"	May have decrements in attention/concentration and executive function Largely reversible with therapy
Subclinical thyrotoxicosis	No consistent increased rates of anxiety or depression Some symptoms may be related to self-knowledge of thyroid disease	Inconsistent associations with mild cognitive decrements Major cognitive decrements not seen May be associated with increased risk for development of dementia

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