

## Letter to the Editor

# Thyroid hormone imbalance and the mechanism by which it causes memory loss

Sir,

Thyroid hormone imbalance is the cause of many cognitive dysfunctions such as memory loss, anxiety and depression. A study conducted by Yu et al suggests that hypothyroidism as well as hyperthyroidism causes depression, anxiety and hippocampal dysfunction in rats.<sup>1</sup> The mechanism of these dysfunctions is not yet completely understood.

Hippocampus is an important structure in the brain associated with learning and memory functions. It contains a high level of thyroid hormone receptors. According to one study conducted by Sahin et al, levothyroxine, which is the most commonly prescribed drug for patients with hypothyroidism, was administered in rats which caused hyperthyroidism and decreased memory performance via decreased expression of GRIN2B gene in the hippocampus. This study also states that cyclin-dependent kinase (Cdk5) plays a crucial role in various neuronal functions and diseases. Cdk5 is activated by Cdk5r1 and Cdk5r2 (two specific binding partners of Cdk5 also known as p35 and p39) to carry out its functions effectively. It plays the main role in synaptic plasticity and memory functions by regulating neurotransmitter release at presynaptic locations and endocytosis of N-methyl-D-aspartate (NMDA) receptors at postsynaptic sites which proves that Cdk5 plays a vital role in modulating communication between neurons which plays a crucial role in processes like learning and memory. Although a lot more research is required to determine the exact mechanism of these dysfunctions it is a great possibility that the dysregulation of Cdk5 activity due to hyperthyroidism contributes to neurological disorders associated with cognitive decline.<sup>2</sup>

As per another study conducted by Taskin et al, rats treated with levothyroxine showed signs of memory deficit along with decreased long-term potentiation (LTP).<sup>3</sup> According to another study by Yu et al, rats were injected with levothyroxine which increased the levels of FT3 and FT4 in serum and hippocampus which impaired long-term fear memory.<sup>4</sup> All of these studies prove that high levels of thyroid hormone cause significant damage to working memory.

Since thyroid hormones contribute to the development of the brain by influencing actin polymerization, microfilament arrangement, and the migration of neurons it should be remembered that while hyperthyroidism

causes memory deficit, individuals with evident hypothyroidism may experience mild to moderate cognitive impairments (particularly affecting memory) as well.<sup>5</sup>

Furthermore, a study conducted by Gobel et al suggests that taking thyroid hormones resulted in higher levels of brain activity, specifically in the right prefrontal cortex and the right parahippocampal region. Although there are numerous studies which state that hyperthyroidism causes cognitive dysfunctions by decreasing brain activity this study proved that when individuals were in a mild hyperthyroid state, compared to when they were in a normal thyroid state, there was a short term increase in brain activity observed during tasks that required memory processing. This heightened activity was noted in several regions including the right supplementary motor area, the right dorsolateral prefrontal cortex, the left rolandic operculum, and the right para-hippocampal gyrus, all of which are known to be involved in memory functions.<sup>6</sup>

This article aims to highlight the significance of the relationship between thyroid hormone imbalance and its adverse effects on working memory. Extensive research should be carried out to find out what level of thyroid hormone causes maximum brain activity and at what exact level does it start causing cognitive dysfunctions. Further research is also imperative to determine the exact mechanism by which thyroid hormone imbalance influences the hippocampus to better understand the significance of keeping thyroid hormone levels within suitable limits through pharmaceutical means.

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