

# **The endocrine system in the progression of mild cognitive impairment to dementia**

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens förvaras i sal Arvid Carlsson, Academicum, Medicinaregatan 3, torsdagen den 16 juni 2022, klockan 9:00

av Patrick Quinlan

Fakultetsopponent:  
Professor Mathias Hallberg  
Uppsala Universitet

## **Avhandlingen baseras på följande delarbeten**

- I. Quinlan P, Horvath A, Wallin A, Svensson J. Low serum concentration of free triiodothyronine (FT3) is associated with increased risk of Alzheimer's disease. *Psychoneuroendocrinology*. 2019;99:112-119.
- II. Quinlan P, Horvath A, Eckerström C, Wallin A, Svensson J. Altered thyroid hormone profile in patients with Alzheimer's disease. *Psychoneuroendocrinology*. 2020;121:104844.
- III. Quinlan, P, Horvath, A, Eckerström, C, Wallin, A, Svensson, J. Higher thyroid function is associated with accelerated hippocampal volume loss in Alzheimer's disease. *Psychoneuroendocrinology*. 2022;139:105710.
- IV. Quinlan P, Horvath A, Nordlund A, Wallin A, Svensson J. Low serum insulin-like growth factor-I (IGF-I) level is associated with increased risk of vascular dementia. *Psychoneuroendocrinology*. 2017;86:169-175.

# The endocrine system in the progression of mild cognitive impairment to dementia

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## **Abstract**

**Background and aims:** Endocrine alterations have been related to cognitive decline, but the role of hormones may vary along the progression to manifest dementia. The overall aim of this thesis was to assess whether thyroid hormones (THs) and insulin-like growth factor-I (IGF-I) are dysregulated around the onset of Alzheimer's disease (AD) and vascular dementia (VaD).

**Methods:** Patients were recruited from the Gothenburg MCI Study. At baseline, THs in serum (Study I – III) and cerebrospinal fluid (CSF, Study II) were evaluated as well as serum IGF-I (Study IV). Brain volumes were determined using magnetic resonance imaging (MRI; Study II and III).

**Results:** In Study I, low serum free triiodothyronine (FT3) was associated with increased risk of progression from subjective cognitive impairment (SCI) or mild cognitive impairment (MCI) to manifest AD. In Study II, serum free thyroxine (FT4) was elevated and FT3/FT4 ratio was decreased in mild AD dementia, whereas CSF TH levels were unchanged. Serum FT3 was associated with higher left amygdala volume in AD patients and total T3 with higher hippocampus volumes in the controls. In Study III, patients with AD and stable MCI displayed reduced serum FT3 and lower FT3/FT4 ratio. Only in AD patients, lower serum thyroid-stimulating hormone (TSH) and higher FT3 and FT3/FT4 ratio were associated with greater annual hippocampal volume loss. In Study IV, patients with low serum IGF-I had a twofold higher risk of conversion to VaD.

**Conclusions:** Overall, the results suggest that dysregulation of THs is associated with hippocampal volume loss and increased risk of progression to AD dementia, whereas altered IGF-I activity may contribute to VaD conversion.

**Keywords:** Thyroid hormones, IGF-I, Alzheimer's disease, vascular dementia