COMMENTARY

Extrathyroidal thyroid hormone synthesis?

Marian Ludgate

School of Medicine, Centre for Endocrine and Diabetes Sciences, Cardiff University, Heath Park, Cardiff CF14 4XN, UK
(Correspondence should be addressed to M Ludgate; Email: ludgate@cf.ac.uk)

Abstract

A paper published in this issue of the *Journal of Endocrinology* has revisited the hypothesis that thyroid hormones may be generated by tissues outside the thyroid gland in higher organisms including mammals. This commentary appraises the strengths and weaknesses of the study, the alternative explanations for the findings and possible future measures to investigate further. The concept of extrathyroidal thyroxine and triiodothyronine synthesis has previously been proposed; by assuming that Nagao et al. and earlier authors are correct, the plausibility and possible mechanisms underlying the hypothesis are discussed.

*Journal of Endocrinology* (2011) 210, 3–4

In a paper entitled ‘Influence of thyroidectomy on thyroxine metabolism and turnover rate in rats’, Nagao et al. (2011) have investigated thyroid hormone kinetics in the hypothyroid state.

In a number of carefully performed studies, which rely on a robust online solid-phase extraction liquid chromatography mass spectrometry (MS)/MS protocol developed by the authors to measure serum thyroxine (T4), triiodothyronine (T3) and reverse T3, they demonstrate that serum levels of all three forms of iodothyronine are decreased but not completely ablated in thyroidectomised rats.

They postulate that deiodination of T4 is enhanced by hypothyroidism to maintain levels of the biologically active thyroid hormone T3 (Kohrle 2000). This could be verified by measuring deiodinase transcripts and enzyme activity in the peripheral tissues of the thyroidectomised rodents compared with euthyroid controls.

Their second, and more controversial, conclusion is that the low levels of thyroid hormone, which persist, are due to extrathyroidal production of iodothyronines. The more mundane explanation, that fragments of thyroid tissue remain, has been excluded by histopathological examination of the trachea, although radio-iodine uptake studies would have provided more solid re-assurance.

An alternative reservoir is reported in studies that indicate a role for the gut flora in absorbing and even deiodinating thyroid hormones (Distefano et al. 1993). To exclude this interesting possible source of the persisting T4 and T3, experiments could be conducted in rodents in which the intestinal bacteria had been reduced by antibiotic treatment.

Assuming that the authors are correct, and that thyroid hormones are produced outside the thyroid, how could this be realised? Thyroid hormone production requires a peroxidase enzyme, a source of iodine, a system to generate H2O2 and a substrate containing tyrosine residues (Vassart & Dumont 1992). In the mammalian thyroid, millennia of evolution have enabled the required components to be optimised in the form of thyroid peroxidase (TPO), the sodium iodide symporter (NIS), the dual oxidases (DUOX) and thyroglobulin (Tg), but alternatives exist.

*Journal of Endocrinology* (2011) 210, 3–4

DOI: 10.1530/JOE-11-0159

Online version via http://www.endocrinology-journals.org

Downloaded from Bioscientifica.com at 11/10/2018 04:58:34AM via free access
produced via catalysis. On the contrary, most vertebrates do possess a thyroid gland; although in the larval stages of the most primitive, thyroid hormones are produced by the endostyle (Crockford 2009); do the experiments of Nagao et al. hint at cells that could be considered to be a vestigial endostyle in higher organisms?

The notion of extrathyroidal hormone production is not new with authors from the sixties, and possibly earlier, providing solid evidence for the process (Evans et al. 1966, Taurog & Evans 1967, Obregon et al. 1981). Most recent evidence reports that in vitro, cardiomyocytes express all of the required components and are able to produce thyroid hormone (Meischl et al. 2008).

Thyroid hormones are essential to the development and maintenance of, for example, the brain and skeletal system and for regulation of the basal metabolic rate (Boelaert & Franklyn 2005); hence, it seems reasonable that higher organisms might have retained a back-up source. Although in vitro models can be very informative, it is hoped that Nagao et al. will extend their in vivo studies in a manner that will convince even the most sceptical thyroidologist and provide insight into the cells/tissues capable of this feat.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

References


Received in final form 24 February 2011
Accepted 3 May 2011
Made available online as an Accepted Preprint 3 May 2011