Investigation of brain GABA levels in hypothyroidism patients by MEGA-Editing proton MR spectroscopy

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Target audiences: Endocrinologist; Neuroscientists

Background: Hypothyroidism is a common endocrine disorder impacting mood and cognition. The accumulated evidence from preclinical studies has indicated that thyroid hormones have effects on multiple components of the γ -aminobutyric acid (GABA) system[1]. GABA, the main inhibitory neurotransmitter in human brain, has been linked to various brain functions. However, research on GABA levels in hypothyroidism seems to be limited.

Purpose: The aim of this proton MR spectroscopy (1H-MRS) study was to investigate whether hypothyroidism is associated with alterations in brain GABA levels.

Methods: 10 hypothyroidism women (age=38.2±7.4 y, range=22-46 y) and 10 matched healthy controls (age=39.3±7.1 y, range=24-47 y) participated in this study. Scans were performed on a 3.0 Tesla Philips scanner. For each subject, a T1-weighted 3D TFE scan was acquired for MRS voxel placement and tissue segmentation. Spectra were recorded from the anterior cingulate cortex /median prefrontal cortex (ACC/mPFC) and posterior cingulate cortex (PCC) using MEGA-PRESS sequence (TR= 2000 ms; TE =68 ms; 256 averages) (Fig. 1). Post-processing of the MEGA-PRESS data was carried out using Gannet v 2.0 toolkit[2]. Unsuppressed water signal was used as a reference for absolute quantification. Because the signal detected at 3.02 ppm is expected to contain contributions from co-edited macromolecules (MM), the signal is labeled GABA+. Since GABA levels differ between gray matter (GM) and white matter (WM), tissue segmentation was performed using an automatic segmentation program, FAST (FMRIB's automated segmentation tool) in the FSL package. All statistical analyses were tested using SPSS v.16.0.

Results: There were no significant group differences in tissue composition in either voxel (all p-values > 0.32). ACC/mPFC GABA+ levels were significantly lower ($p = 0.003$) in hypothyroidism women (1.13 ± 0.05 IU) compared to healthy controls (1.25 ± 0.10 IU), whereas no significant difference ($p=0.41$) was observed in the PCC (Fig. 2). Lower ACC/mPFC GABA+ remained significant after controlling for age and GM:WM ratio.

Discussion/Conclusion: To our knowledge, this study is the first to report decreased brain GABA+ in hypothyroidism. The abnormal thyroid hormones may be associated with dysfunctional synthesis and metabolism of GABA[1], although the details remain to be elucidated. Altered GABA neurotransmission may be an important neurobiological mechanism underlying neuropsychiatric and cognitive changes in hypothyroidism. Our study helps to better understand thyroid-brain interaction in hypothyroidism, however, future studies are needed to confirm and interpret our preliminary findings.

References:

1. Wiens, S. C. Trudeau, V. L. Thyroid hormone and gamma-aminobutyric acid (GABA) interactions in neuroendocrine systems. Comparative Biochemistry and Physiology. 2006; Part A 144: 332–344

2. Edden, Richard A. E., et al. Gannet: A batch-processing tool for the quantitative analysis of gamma-aminobutyric acid-edited MR spectroscopy spectra. Journal of Magnetic Resonance Imaging. 2013; doi: 10.1002/jmri.24478.

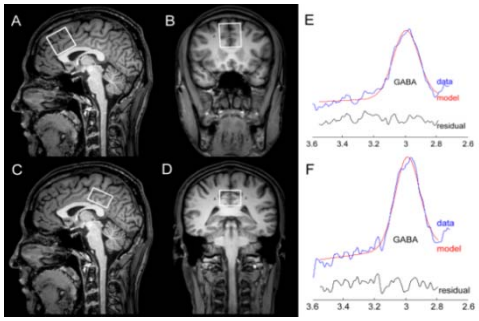

Fig.1. Voxel placement and resulting spectra. (A,B) and (C,D) show the positions of ACC/mPFC (3x3x3cm^3) and PCC (3x3x2cm^3) VOIs. (E,F) show the curve-fitting of the GABA+ peaks using Gannet toolkit.

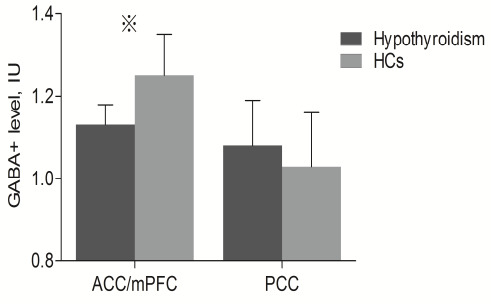

Fig.2. Comparisons of GABA+ levels in ACC/mPFC and PCC between hypothyroidism women and healthy controls. A significant decrease in ACC/mPFC was detected (※ represents $p<0.05$).