

Brain, mood and cognition during treatment initiation in mild hypothyroidism

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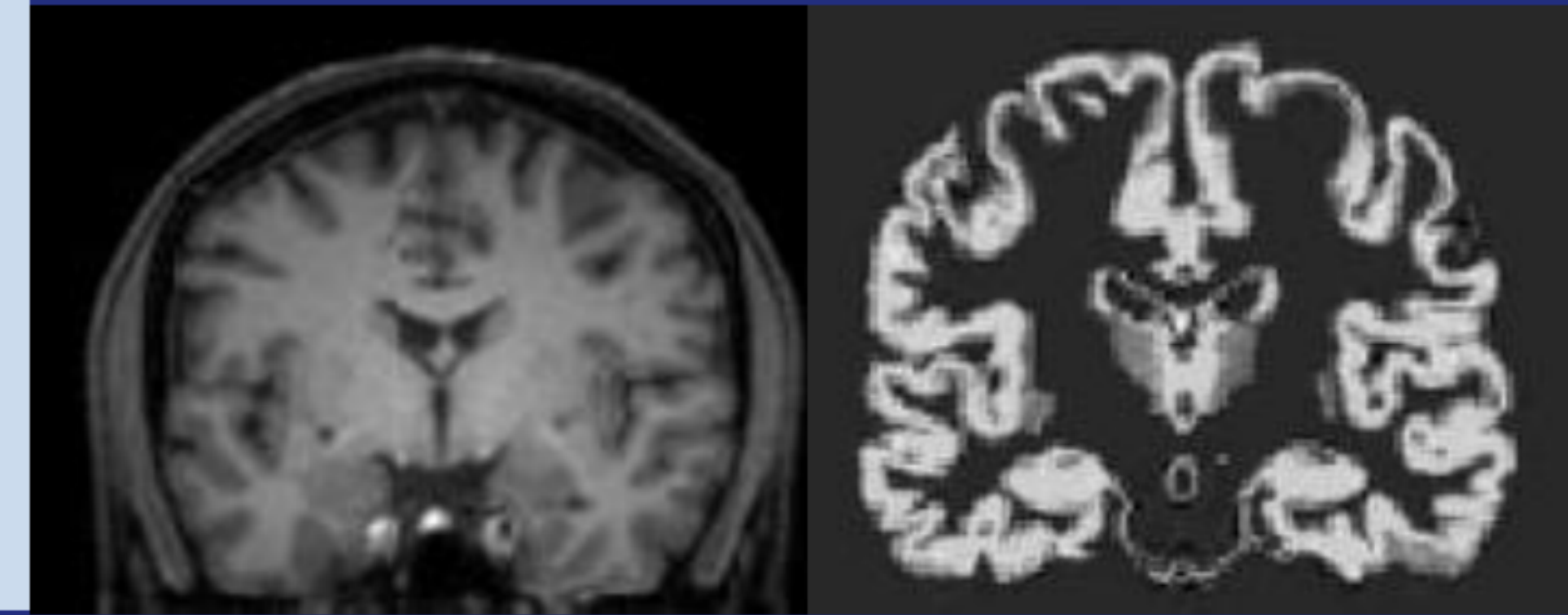
Introduction

Animal studies (Alzoubi et al. 2009) and first human brain imaging studies (Bauer et al. 2009) suggest neural involvement in affective and cognitive symptoms of hypothyroidism. Here, we introduce non-invasive magnetic resonance imaging (MRI) that allows the investigation of brain structure and functional connectivity between brain regions in living patients. Thereby, we try to identify neural correlates of hypothyroid symptoms.

Methods

9 patients and 9 healthy matched control subjects underwent structural and resting-state functional 3T MRI scanning and comprehensive neuropsychological testing before and 3 months after treatment initiation. Voxel-based-morphometry (Ashburner & Friston, 2000) was used to investigate grey matter density and resting-state functional MRI (Fox & Raichle, 2007) to analyse the connectivity between brain regions known to be involved in hypothyroidism such as the hippocampus, the amygdala and the anterior cingulate cortex (Bauer et al. 2009). Groups were compared on all measures pre- and posttreatment. Changes specific to the patient group were assessed by paired t-tests and the interaction between group and time. Affective symptoms were additionally correlated with brain structure and function.

Figure 1 T1-weighted structural MR image and gray matter segment for voxel-based morphometry.



Results

- Treatment restored thyroid hormone levels to the reference range.
- Patients reported significantly higher symptom load, reduced well-being and mental health compared to the control group before treatment.
- Mood alterations reversed with treatment.
- The observed mood alterations could not be related to brain structure or function.
- We did not find impairment in memory, working memory, attention or psychomotor speed and no change with treatment.
- We did not find structural or functional brain alterations even before treatment and no change with treatment.

Table 1 Descriptive (mean±SD) and statistical (p-values) results of patient and control group pre- and posttreatment initiation.

Sample characteristics	Patient group (n=9)		Control group (n=9)		Group comparison		Change in patients	Interaction group*time
Age (years)	42±5		38±8		n.s.			
Sex	1 male		1 male		--			
Intelligence (IQ)	104±10		107±8		n.s.			
Serum thyroid hormone levels	pre	post	pre	post	t-test pre	t-test post	paired t-test	ANOVA
TSH (mU/l)	6.1±1	3.4±1	2.9±1	2.5±1	<.01	n.s.	<.01	<.01
ft3 (pmol/l)	4.8±1	4.6±1	4.5±1	4.4±0.4	n.s.	n.s.	n.s.	n.s.
ft4 (pmol/l)	12.6±2	15.7±2	14.9±1	14.5±1	<.05	n.s.	<.01	<.01
TPO-ab (U/ml)	285±184	287±184	11±2	9±3	<.01	<.01	n.s.	n.s.
Patient-reported outcomes								
Beck depression scale	6.0±5	3.0±2	2.8±3	2.6±2	n.s.	n.s.	n.s.	n.s.
Hamilton depression scale	6.4±4	2.6±2	3.8±3	2.6±2	n.s.	n.s.	<.01	n.s.
Well-being questionnaire-12	23±5	27±4	29±3	30±4	<.05	n.s.	<.05	n.s.
Symptom Check List-90	1.3±0.2	1.1±0.1	1.2±0.2	1.1±0.1	n.s.	n.s.	<.05	n.s.
Short Form 36 – physical	55±6	53±10	55±4	55±3	n.s.	n.s.	n.s.	n.s.
Short Form36 – mental	45±8	52±5	52±5	51±5	<.05	n.s.	<.05	<.05
Thyroid Symptom Rating (ThySRQ)	6.9±3	3.8±2	2.8±2	3.2±2	<.01	n.s.	<.01	<.05
Thyroid-related Quality of Life (ThyDQoL)	1.2±0.7	1.8±0.7	1.6±0.7	1.6±0.6	n.s.	n.s.	<.05	<.05

Conclusions

We did not find evidence in favour of neural alterations in mild hypothyroidism, contrasting positive findings in severe hypothyroidism (Bauer et al. 2009; Singh et al. 2013). The observed mood normalisation most likely mirrors a placebo effect as it has only been shown in control group comparisons, but not in placebo-controlled trials (Dayan and Panicker, 2013). Our findings are in line with recent well-powered population-based studies that fail to show affective and cognitive symptoms in mild incidentally detected hypothyroidism, but report affective symptoms in known hypothyroidism irrespective of the thyroid hormone status (Jørgensen et al. 2014; Samuels et al. 2014). Reported affective symptoms in known adequately treated hypothyroidism (Quinque et al. 2013, 2014) thus more likely derive from unspecific factors such as labelling. Our MRI data is available for use in meta-analyses here: <http://neurovault.org/collections/169>.

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Thyroid non-cancer

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