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Letter to the editor

Cognitive function in Hashimoto's thyroiditis under levothyroxine treatment

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ABSTRACT

OBJECTIVE: Although overt hypothyroidism has been documented as exerting detrimental effects on cognition and behavior, it remains controversial whether subclinical hypothyroidism or euthyroid patients with Hashimoto's thyroiditis (HT) under levothyroxine (LT4) treatment may experience any noticeable decline in cognitive function. PATIENTS: Two otherwise healthy, highly-functioning, first-degree relatives with a diagnosis of HT, under LT4 treatment for two years, were prospectively recruited into a clinical research study setting and followed for a year. MEASUREMENTS: Thyroid functions tests and a detailed battery of tests assessing global cognitive status, attention, verbal and working memory, visuoperceptual skills, executive functions and mood were performed at baseline and at one year after recruitment. RESULTS: Overall, patients' performance on the neuropsychological battery was good and, in the majority of cognitive functions, their performance could be characterized as exceptional. No noticeable changes in any of the studied parameters were detected. CONCLUSIONS: The present case study failed to detect any noticeable changes in the cognitive and emotional function of two women with HT under LT4 treatment. The course of cognitive function of the two HT patients, evaluated by a detailed battery of tests, tends to confirm the benign nature of HT.

Key words: Hashimoto's thyroiditis, Neuropsychology, LT4 treatment

Chronic autoimmune (Hashimoto's) thyroiditis (HT) is the most common thyroid disorder in iodine-sufficient areas. HT is marked by the presence of complement-fixing autoantibodies to thyroid peroxidase (TPOabs) which tend to correlate with progressive thyroidal damage[1] and may lead to subclinical and overt hypothyroidism. Thyroid hormone deficiency (overt hypothyroidism) has profound and multi-systemic detrimental effects from which brain and behavior are not spared. The latter may relate to global cognitive, behavioral and emotional changes, including depression.[2] This is not the case for subclinical hypothyroidism and euthyroid HT, whether under levothyroxine (LT4) treatment or not, the effect of which on cognitive performance is somewhat controversial. Whereas it has been suggested that "a state of brain hypothyroidism in the context of systemic

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euthyroidism"[3] and an association between thyroid autoimmunity and cognitive function may exist,[4] and that neurocognitive functioning and psychological well-being may not be completely restored in patients with hypothyroidism despite LT4 treatment,[5] neither was an association between indices of depression and thyroid autoimmunity established in a population study[6] nor did treatment with levothyroxine for a year improve any parameters of cognitive functioning in patients with subclinical hypothyroidism.[7]

Our aim was to test: 1) whether LT4 treatment improves the profile of first degree relatives as to different aspects of cognition and emotion, and 2) whether euthyroidism under LT4 treatment (and manifesting with depressive symptomatology) leads to neuropsychological deficits.

Two otherwise healthy, highly-functioning, first-degree relatives [daughter (A) and mother (B)] with a diagnosis of HT under LT4 treatment were recruited into a clinical research study setting.

Patient A, at the time of the first neuropsychological testing (initial assessment in 2010) was a 25-year old, right-handed woman on therapy for Hashimoto's thyroiditis during the last two years. She was a Social Sciences postgraduate student of a Greek university and had had her first neuropsychological examination because of personal complaints concerning her low mood and experiences of fatigue, but also due to fears about the diagnosis of her disease.

Patient B, the mother of patient A, was a right-handed woman, 62 years old at the time of the initial examination. She was first diagnosed with Hashimoto's thyroiditis five years previously, whereas treatment was instituted two years ago (due to self-perceived physical and cognitive disturbances). Patient B, a divorced woman, had completed sixteen years of education (including university studies), which she completed—as had her daughter—with honors and distinction.

The women shared a familial history of relatives suffering from thyroid disorders (e.g. goiter). Neither woman had been diagnosed with other somatic health problems, with the exception of patient A's irregular menstrual cycle. The two patients at the time of the two examinations (test and retest after a year's interval) repeated their thyroid hormone function tests.

Both patients were on treatment with synthetic T4 (levothyroxine sodium): patient A was on a daily dose of 62mcg, which after TSH re-assessment was modified to 88mcg and patient B had been on 100mcg for two years before the initial examination.

At baseline, a detailed neuropsychological assessment (including evaluation of attention, verbal memory, working memory, visuoperceptual skills and executive functions) was carried out along with a brain magnetic resonance and an assessment of the patients' thyroid function status (chemiluminescent immunoassay). Full neuropsychological assessment and selected thyroid functions tests were repeated one year after the recruitment.

Results of the cognitive and emotional examination (test and retest) along with thyroid function tests are summarized in Table 1 and 2, respectively. At baseline, patient B was found to be over-treated. The emotional profile of both women suggested depressive symptomatology. On the basis of the finding of a collection of signs and symptoms (DSM-IV-TR criteria), patient A was also diagnosed with major depressive disorder. Computerized tomography (CT) and magnetic resonance imaging (MRI) at the time of the first neuropsychological examination were normal for both women with no detectable brain damage. Overall, patient A's and B's performance on the neuropsychological battery was good and in the majority of cognitive functions their performance could be characterized as exceptional. No noticeable changes in any of the studied parameters were detected.

The present case study failed to detect any noticeable changes in the cognitive function of two women with HT under LT4 treatment. The course of cognitive function of the two HT patients, evaluated by a detailed battery of tests, tends to confirm the benign nature of HT. Notably, patient A, who was diagnosed with major depressive disorder and was thus expected to demonstrate cognitive impairment (mainly deficits in attention, memory and executive functioning), was found to be resistant to even subtle changes. Patient B was also found to lack psychomotor slowing and impairments in memory and executive functioning. These are unusual and reassuring findings, which are in

Table 1. Summary of cognitive and emotional examination for patients A and B (first assessment and at one-year follow-up)

Tests	First assessment A	Follow-up A	First assessment B	Follow-up B
Global Cognitive Status				
Mini-Mental State Examination	30/30	30/30	29/30	30/30
Attention				
Trail-Making Test Part A	80th percentile	>90th percentile	80th percentile	80th percentile
Ruff 2 & 7 Selective Attention Test				
Automatic detection speed	95th percentile	95th percentile	95th percentile	95th percentile
Automatic detection accuracy	95th percentile	95th percentile	95th percentile	95th percentile
Controlled search speed	95th percentile	95th percentile	95th percentile	95th percentile
Controlled search accuracy	95th percentile	95th percentile	95th percentile	95th percentile
Digit Span Forward	10	9	8	9
Stroop Word	80th percentile	90th percentile	80th percentile	80th percentile
Color	80th percentile	90th percentile	80th percentile	80th percentile
Color/Word	80th percentile	90th percentile	80th percentile	80th percentile
Spatial Span	8	8	6	7
Verbal Memory				
Word List Learning Immediate	37/40	38/40	35/40	33/40
Delayed	8/10	9/10	7/10	7/10
Word recognition	20/20	20/20	20/20	20/20
Stories Learning Immediate	16/16	15/16	15/16	16/16
Delayed	15/16	15/16	14/16	15/16
Working Memory				
Trail-Making Test Part B	80th percentile	80th percentile	80th percentile	80th percentile
Digit Span Backward	7	8	7	5
Visuoperceptual Skills				
Rey-Osterrieth Complex Figure Immediate Recall	35/36	35/36	33/36	32/36
Delayed Recall	34/36	35/36	30/36	32/36
Recognition	12/12	12/12	12/12	12/12
Executive Functions				
Semantic Fluency (total number of words)	90th percentile	90th percentile	80th percentile	80th percentile
Phonological Fluency (total number of words)	80th percentile	90th percentile	90th percentile	90th percentile
Mood				
Center for Epidemiologic Studies-Depression Scale	40/60	43/60	15/60	Declined
Geriatric Depression Scale	-	-	5/15	4/15

discordance with previous reports not only for patients with HT and on LT4 treatment[5] but also for patients suffering depressive symptomatology[8] in whom poor performance (below normal) in various domains of neurocognitive functioning have been tentatively determined. These hypotheses should be further investigated in future quantitative experimental studies. Furthermore, according to Panicker,[9] various types of thyroid dysfunction (e.g. hypothyroidism) are usually found in first-degree relatives, such as mothers and daughters. A similar hypothesis in genetics has been proposed as regards IQ[10] where correlations between sons with their fathers' IQs are the lowest (r=.44), while the correlations between mothers and daughters' IQs are the highest [at about r=.68]. Accordingly, a potential objective for future research is to focus on

Table 2. Thyroid function tests for patients A and B (first assessment and at one-year follow-up)

	Normal values	First assessment A	Follow-up A	First assessment B	Follow-up B
BMI (kg/m^2)		22	22	23	23
TSH (μIU/ml)	0.3 - 5	2.57	0.49	0.02	0.23
fT4 (ng/dl)	0.8 - 2	1.22		1.62	
fT3 (pg/ml)	2 - 4.8	3		2.84	
T4 (μg/dl)	5 – 12		6.43		
Anti-TPO (IU/ml)	0 – 100	3700	584	1680	2300
Anti-TG (IU/ml)	0 – 150	351	275	>4000	>4000
B12 (ng/ml)	200 – 870	393	400	374	400

Anti-TG: thyroglobulin antibodies; Anti-TPO: thyroid peroxidase antibodies; BMI: body mass index; B12: vitamin B12; fT4: free thyroxine; fT3: free triidothyronine; T4: thyroxine; TSH: thyrotropin.

unveiling the way(s) that first-degree relatives react to hormonal supplements and changes in their cognitive status, which may be linked in some hereditary genetic way, especially with regard to female relatives.

CONFLICT OF INTEREST

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