ON THE PATHOGENESIS OF PSYCHIC DISORDERS IN HASHIMOTO'S THYROIDITIS

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Introduction. Autoimmune thyroiditis (AIT) is a most highly spread endocrine disease, gradually destroying thyroid by T-cell- and antibody-mediated mechanisms [1]. Thyroid hormones control neurogenesis in fetal and adult brain, deeply influencing functions of neurons and glia [2]. Moreover, brain and thyroid share common antigens. R. Asher gave a classical description of "myxoedematous madness" related to hypothyroidism [3]. Mental disorders in AIT vary - from light phobiae and episodes of depression to delirium and hallucinations. However, to date, the pathogenesis of neuropsychiatric manifestations in AIT remains unclear, with possible roles of autoantibodies against several common or cerebral antigens and impact of hormonal/metabolic changes (hypothyroidism with hyperprolatinaemia, hypocalcaemia etc). Meanwhile, the existance of obscure "Hashimoto's encephalopathy" was postulated [1].

Aims. To reveals connection between psychic disorders in AIT and various metabolic and immunoendocrinological effectors.

Material and methods. We examined 1929 patients with AIT [confirmed by diagnostic criteria of Japanese Thyroidological Association [4]] accompanied by hypothyroidism of varying severity, analyzing their complaints, anamnesis and clinical manifestations of the disease, plasma levels of TSH, thyroid hormones, total and ionized calcium, inorganic phosphate. The content of vitamin D3 (cholecalciferol) was checked in 150 cases of AIT. In addition special subgroup of 17 patients with AIT and verified psychiatric diagnoses (mostly, schizophrenia) were compared to 21 AIT patients without psychic disorders and 20 healthy donors (age and sex-matched) by the following parameters, measured by ELISA: blood levels of thyrotopin (TSH), free thyroxin, free 3-iodothyronin, prolactin, autoantibodies towards thyroglobulin and thyroperoxidase and also the size of thyroid gland measured by ultrasonography. IgG was isolated from sera of most severe comorbid AIT/psychiatric patients by affinity chromatography on column with protein G and injected intracysternally to brain of mice with subsequent open field behavior test protocol against IgG of healthy donors injected as a control.

Results. In a general group of AIT patients 25,5% suffered from various phobiae, which is 3,5 times greater frequency compared to prevalence of phobiae among general local population. Presence of phobiae correlated to lover levels of ionized calcium, higher content of inorganic phosphate and lower level of D3 vitamin in AIT patients. Its seasonal variance corresponded to the seasonal fluctuations of vitamin D3 content. Comparing the comorbid cases of psychic disorders and AIT with pure AIT cases and healthy donors, we registered that the levels of TSH, FT4, prolactin, estrogens and antibodies against thyroglobulin as well as the size of thyroid gland were associated with various manifestations of mental disorder. The levels of antibodies to thyroperoxidase positively correlated to clinical signs of hypothyroidism and to the thyroid size. Injection of IgG taken from severe combined AIT/psychiatric patients into mice brain provoked disorders of behavior in open field tests.

Conclusion. Both endocrine and immune effectors may cause mental disorders in AIT.

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IN SEARCH OF LINKS BETWEEN ALZHEIMER'S DISEASE AND HASHIMOTO'S THYROIDITIS

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Introduction. Pathologic prevalence of dementia increases worldwide, it already involves up to 50 million people. The premier reason of it still is the Alzheimer's disease. Global prevalence of Hashimoto's chronic autoimmune thyroiditis also progresses rapidly, making it most highly spread autoimmune disorder of nowadays. Earlier several researchers came to conclusion that both hyperthyroidism and hypothyroidism may be related to higher risk of Alzheimer's disease [1]. We demonstrated that microglial phagocytic activity in CNS is controlled by thyroid hormones [2], as well as many metabolic and morphogenetic processes in brain.

Aims. To explore probable relationships between Hashimoto's thyroiditis and Alzheimer's disease checking early extracerebral expression of Alzheimer's marker among patients with Hashimoto's disease, but without any Alzheimer's clinical signs.

Material and methods. We took a scraping of buccal epithelium (BE) for the detection of pre-clinical marker of Alzheimer's disease - the Tau protein (TP). By special technic [3] the immunofluorescence analysis of samples was performed with confocal microscope 1000B (Japan), the data obtained were processed via ImageJ program. The main group of patients included 7 persons (6 females) without any clinical signs of Alzheimer's disease, but with diagnosis of Hashimoto thyroiditis, established according modified criteria of Japanese Thyroidological Association [4] and being under treatment with "Euthyrox©" (L- thyroxine) or "Thyrozol©" aged from 8 to 77 years old. Control group included 8 apparently healthy persons (7 females) aged from 10 to 75. Also we compared dental status

of control and main groups, using conventional dental indexes and scales of cavities and periodontitis. Thyroid hormones, thyrotropin and anti-thyroid antibodies level in blood was measured by ELISA.

Results. TP expression was verified in BE in 100% of Hashimoto's thyroiditis patients [average level of expression was 17,51 conventional units (CU)], while in control group the test was negative with the average level of expression 0,35 CU ($p < 0.001$ with main group). No difference between groups in dental status was revealed, which rules out possible local reasons for their difference in TP expression. TP expression level did not correlate to age or sex of patients, neither to their blood level of thyroid hormones.

Conclusion. There is a relation between preclinical expression of TP and Hashimoto's thyroiditis. The buccal expression of TP precourses the first clinical manifestations of Alzheimer's disease.

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PATIENTS WITH ATOPY EXHIBITED ATTENUATED NEUROENDOCRINE RESPONSE DURING PSYCHOSOCIAL STRESS

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Introduction. Chronic stress events may result in worsening the quality of life and consequent pathological states. Accordingly, psychosocial stress may represent a factor involved in both the onset of atopic disorders and the exacerbation of existing atopic disease. In patients with atopy, a decreased responsiveness of the hypothalamic-pituitary-adrenocortical axis to stress stimuli has been documented.

Aims. The aim of the present study was to test the hypothesis that the blunted cortisol response to psychosocial stress in atopic patients is associated with changes in salivary alpha-amylase and aldosterone using a psychosocial stress procedure based on public speech.

Methods. The study was performed in 106 subjects of both sexes, 53 atopic patients suffering from allergic rhinitis, allergic asthma or atopic dermatitis and 53 age-, sex-, the menstrual cycle phase- and BMI- matched healthy controls.

Results. Substantially attenuated activity of alpha-amylase and reduced secretion of aldosterone during the psychosocial stress were observed in the whole sample of patients with atopy. Higher activity of alpha-amylase observed in the follicular compared to the luteal phase in healthy women was not present in atopic patients. In both males and females, atopy was associated with blunted cortisol response but unchanged heart rate. Psychological characterization revealed a significantly higher trait anxiety and higher preference for avoidance-oriented coping strategy in female but not male atopic patients.

Conclusion. These findings provide evidence that patients with atopy exhibit insufficient alpha-amylase and aldosterone responsiveness to psychosocial stressor, thus suggesting decreased sympathetic activity. Changes in personality traits were demonstrated in female atopic patients, but not in male patients.

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PUPILLOMETRY IN ADOLESCENT DEPRESSION

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Introduction. Major depressive disorder is associated with abnormal autonomic regulation. Pupillary light reflex (PLR) - pupil constriction in response to luminance increases - represents a non-invasive investigative method of sympathetic and parasympathetic autonomic nervous system activity in the context of psychophysiological processes (i.e. attention) [1,2].

Aims. The aim of our study was to estimate PLR changes in response to mental stressor - Go/NoGo test in the group of adolescent patients suffering from depressive disorder.

Methods. 25 adolescent patients with major depressive disorder (average age: $15,2 \pm 0,3$ years) and 25 healthy subjects same age and gender were examined in psychophysiological laboratory under standard conditions (quiet darkened room, same light intensity, temperature 22 - 23 °C) in the morning after light breakfast. Absolute and percentage values of pupil size changes were assessed during the rest phase and after application of mental stressor, separately for both eyes using a handheld infrared optical scanner Pupillometer PLR-2000 (NeurOptics, USA).

Results. PLR reactivity was significantly lower in patients suffering from major depressive disorder compared to healthy group after application of Go/NoGo test (right side: -25% vs. -29%, $p = 0,014$; left side: -25% vs. -29%, $p = 0,012$). No significant between-groups differences were assessed in the basal value of the pupil size.

Conclusion. Lower PLR reactivity can point to discrete abnormalities in autonomic nervous system regulation in the context of deficient parasympathetic activity and tendency to prevalence of sympathetic activity in adolescent major depressive disorder. These findings are in accordance with lower cardiovagal regulation in adolescent depression [3]. Therefore, we suggest that our findings of central autonomic dysregulation could contribute to understanding of potential pathomechanisms in adolescent depressive disorder.

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