

# RESULTS

## Thyroid activity

### Used studies and Abstracts

- 1) V. G. Alexeev, . L. V. Kuznekova EIS System (Galvanic Skin responses measurement device) in adjunct to Treatments' monitoring and to diagnosis with the conventional methods. Botkin 2006

#### **Abstract**

*Clinical investigations were conducted at the S.P. Botkin Hospital from May 20, 2006, to September 1, 2006, in order to evaluate the Bioimpedance parameters provide from a device named Electro Interstitial Scan (E.I.S), we performed drug administration studies. These patients presented hypothyroidism diagnosed by laboratory tests (hypothyroidism N= 52), and were undergoing no treatment. The treatment follow-up being undertaken on one hand with the EIS System and on the other hand by conventional methods.*

#### **Thyroid treatment monitoring**

*The findings show that SDC 11/12 and TSH has a significant negative correlation to each other ( $r = -0.975$ ,  $p = 0.005$ ). It shows that, SDC 11/12 shares approximately 95.1% (that is  $(-0.975)^2 \times 100\%$  or  $0.951 \times 100\%$ ) of its variability with TSH. Thus, a high value of SDC 11/12 corresponds to low TSH or low value of SDC 11/12 corresponds to high TSH. The findings show that EPA-SPA11/12 and TSH has a significant positive correlation to each other ( $r = 0.926$ ,  $p = 0.024$ ). It shows that, EPA-SPA11/12 shares approximately 85.7% (that is  $(0.926)^2 \times 100\%$  or  $0.857 \times 100\%$ ) of its variability with TSH. Thus, a high value of EPA-SPA11/12 corresponds to high TSH or low value of EPA-SPA 11/12 corresponds to low TSH.*

2)Jin-Long Chen; Hung-Wen Chiu; Yin-Jiun Tseng; Woei-Chyn Chu. Hyperthyroidism is Characterized by Both Increased Sympathetic and Decreased Vagal Modulation of Heart Rate: Evidence From Spectral Analysis of Heart Rate Variability Clin Endocrinol. 2006;64(6):611-616

*Abstract*

*Objective:* The clinical manifestations of hyperthyroidism resemble those of the hyperadrenergic state. This study was designed to evaluate the impact of hyperthyroidism on the autonomic nervous system (ANS) and to investigate the relationship between serum thyroid hormone concentrations and parameters of spectral heart rate variability (HRV) analysis in hyperthyroidism. *Design and patients* Thirty-two hyperthyroid Graves' disease patients (mean age 31 years) and 32 sex-, age-, and body mass index (BMI)-matched normal control subjects were recruited to receive one-channel electrocardiogram (ECG) recording.

*Measurements:* The cardiac autonomic nervous function was evaluated by the spectral analysis of HRV, which indicates the autonomic modulation of the sinus node. The correlation coefficients between serum thyroid hormone concentrations and parameters of the spectral HRV analysis were also computed.

*Results:* The hyperthyroid patients revealed significant differences ( $P < 0.001$ ) compared with the controls in the following HRV parameters: a decrease in total power (TP), very low frequency power (VLF), low frequency power (LF), high frequency power (HF), and HF in normalized units (HF%); and an increase in LF in normalized units (LF%) and in the ratio of LF to HF (LF/HF). After correction of hyperthyroidism in 28 patients, all of the above parameters were restored to levels comparable to those of the controls. In addition, serum thyroid hormone concentrations showed significant correlations with spectral HRV parameters.

*Conclusions* Hyperthyroidism is in a sympathovagal imbalanced state, characterized by both increased sympathetic and decreased vagal modulation of the heart rate. These autonomic dysfunctions can be detected simultaneously by spectral analysis of HRV, and the spectral HRV parameters could reflect the disease severity in hyperthyroid patients.

3)Maciel, B.C., Gallo, L. Jr, Marin Neto, J.A., Maciel, L.M.Z., Alves, M.L.D., Paccola, G.M.F. & Iazigi, N. (1987) The role of the autonomic nervous system in the resting tachycardia of human hyperthyroidism. Clinical Science, 72, 239–244.

*Abstract:*

*The mechanisms that control resting heart rate in hyperthyroidism were evaluated in six patients before and after treatment with propylthiouracil. The patients were subjected to pharmacological blockade under resting conditions in two experimental sessions: first session, propranolol (0.2 mg/kg body weight); second session, atropine (0.04 mg/kg body weight) followed by propranolol (0.2 mg/kg body weight). All drugs were administered intravenously. Resting heart rate was significantly reduced from 100  $\pm$  6.5 beats/min to 72  $\pm$  2.5 beats/min ( $P$  less than 0.005) after clinical and laboratory control of the disease. After double blockade, intrinsic heart rate was reduced from 105  $\pm$  6.8 beats/min before treatment to 98  $\pm$  6.0 beats/min after treatment ( $P$  less than 0.025). The reduction in heart rate caused by propranolol was not significantly different before (-13  $\pm$  1.4 beats/min) and after (-9  $\pm$  1.0 beats/min) propylthiouracil. In contrast, atropine induced a higher elevation of heart rate after treatment (45  $\pm$  8.6 beats/min) than before treatment (26  $\pm$  4.0 beats/min). The present results suggest no appreciable participation of the sympathetic component of the autonomic nervous system in the tachycardia of hyperthyroidism, at least under the conditions of the present study. The small change observed in intrinsic heart rate, although significant, seems to indicate that this is not the most important mechanism involved in this tachycardia. Our results suggest that an important reduction in the efferent activity of the parasympathetic component participates in the mechanisms that modify resting heart rate in hyperthyroidism.*

- 4) Inukai, T., Takanashi, K., Kobayashi, H., Fujiwara, Y., Tayama, K., Aso, Y. & Takemura, Y. (1998) Power spectral analysis of variations in heart rate in patients with hyperthyroidism or hypothyroidism. *Hormone and Metabolic Research*, 30, 531–535.

**Abstract**

*Power spectral analysis (PSA) of the variation in heart rate is useful in determining the relative activity of the sympathetic and parasympathetic nerves. In this study, PSA was used to investigate the relationship between abnormalities in autonomic nerve function and the presence of thyroid disorders in patients with autoimmune thyroid diseases. The low frequency (LF) or high frequency (HF) components of R-R variations were determined by PSA. The coefficient of variation of the R-R time intervals (CV(R-R)) was positively correlated with HF in healthy subjects. In untreated hyperthyroid patients with Graves' disease, the CV(R-R) and HF values were significantly lower than in healthy controls. Moreover, the LF/HF ratio in patients with untreated Graves' disease was significantly higher, and the LF/HF ratio in hypothyroid patients with Hashimoto's thyroiditis was significantly lower than in healthy controls. A negative correlation was observed between serum levels of free thyroid hormones (FT4 and FT3) and HF in Graves' disease patients. In some hyperthyroid patients, antithyroid drug therapy or beta-blocker administration gradually restored reduced HF values. Present results suggest that relative vagal nerve activity is reduced in hyperthyroid patients and that this reduction is reversible according to the decrease in serum levels of thyroid hormones.*

- 5) Girard, A., Hugues, F.-C., Le Jeune, C. & Elghozi, J.-L. (1998) Short-term variability of blood pressure and heart rate in hyperthyroidism. *Clinical Autonomic Research*, 8, 181–186.

**Abstract**

*The effect of hyperthyroidism on the short-term memory variability of blood pressure and heart rate was evaluated in 12 untreated hyperthyroid patients during thyrotoxicosis and after a 6 1/2 month treatment designed to achieve a stable euthyroid state. Beat-by-beat finger blood pressure was measured with a Finapres device. The pulse interval, from which pulse rate was derived, was obtained from the blood pressure signal. Due to the significant change in heart rhythm associated with thyrotoxicosis, both pulse interval (taken as a surrogate of heart period) and pulse rate (taken as a surrogate of heart rate) were computed. Power spectral analysis showed a reduction in the overall heart period variability in the supine position in the hyperthyroid compared to the euthyroid state. This effect was observed in the low-frequency (0.005-0.068 Hz), mid-frequency (0.068-0.127 Hz) and high-frequency (respiratory) domains as well, with a significant reduction of the modulus of these bands of 31%, 35% and 47%, respectively. The heart rate spectral modulus also exhibited a reduction of the high-frequency component (31%) in the supine position in the hyperthyroid subjects. These changes in heart rhythmicity corroborate a vagal deficit in hyperthyroidism. In addition, blood pressure spectral power exhibited a significant deficit in the orthostatism-induced mid-frequency systolic blood pressure rise in the hyperthyroid state (64%) compared with the euthyroid state. This observation may reflect a reduced vascular sympathetic activation with standing. The resulting vasodilatation could well contribute to normalize blood pressure in thyrotoxicosis in which cardiac output is increased.*

- 6) Burggraaf, J., Tulen, J.H.M., Lalezari, S., Schoemaker, R.C., De Meyer, P.H.E.M., Meinders, A.E., Cohen, A.F. & Pijl, H. (2001) Sympathovagal imbalance in hyperthyroidism. *American Journal of Physiology. Endocrinology and Metabolism*, 281, E190–E195.

**Abstract**

*We assessed sympathovagal balance in thyrotoxicosis. Fourteen patients with Graves' hyperthyroidism were studied before and after 7 days of treatment with propranolol (40 mg 3 times a day) and in the euthyroid state. Data were compared with those obtained in a group of age-, sex-, and weight-matched controls. Autonomic inputs to the heart were assessed by power spectral analysis of heart rate variability. Systemic exposure to sympathetic neurohormones was estimated on the basis of 24-h urinary catecholamine excretion. The spectral power in the high-frequency domain was considerably reduced in hyperthyroid patients, indicating diminished vagal inputs to the heart. Increased heart rate and mid-frequency/high-frequency power ratio in the presence of reduced total spectral power and increased urinary catecholamine excretion strongly suggest enhanced sympathetic inputs in thyrotoxicosis. All abnormal features of autonomic balance were completely restored to normal in the euthyroid state.  $\beta$ -Adrenoceptor*

antagonism reduced heart rate in hyperthyroid patients but did not significantly affect heart rate variability or catecholamine excretion. This is in keeping with the concept of a joint disruption of sympathetic and vagal inputs to the heart underlying changes in heart rate variability. Thus thyrotoxicosis is characterized by profound sympathovagal imbalance, brought about by increased sympathetic activity in the presence of diminished vagal tone.

7) Coulombe, P., Dussault, J.H. & Walker, P. (1976) Plasma catecholamine concentrations in hyperthyroidism and hypothyroidism. *Metabolism: Clinical and Experimental*, 25, 973-979

#### Abstract

Using a modification of the fluorometric method of Anton and Sayre,<sup>4</sup> we have measured the plasma epinephrine (E) and norepinephrine (NE) concentrations in patients with thyroid dysfunction. There was no significant difference in plasma E in hyperthyroid or hypothyroid subjects, the values being similar to those observed in normal subjects. There was a striking relationship between age and plasma NE in the euthyroid individuals ( $r = 0.685$ ,  $p < 0.001$ ,  $N = 41$ ). Observed plasma NE concentrations were similar in control subjects ( $21.05 \pm 1.6$  ng/100 ml; mean  $\pm$  SEM) and hyperthyroid patients ( $22.33 \pm 2.0$  ng/100 ml). However, plasma NE was significantly increased in hypothyroidism ( $35.46 \pm 3.9$  ng/100 ml;  $p < 0.01$ ) and remained statistically different when the age factor was excluded ( $31.31 \pm 2.67$  ng/100 ml;  $p < 0.025$ ). There was no correlation between plasma NE and serum thyroxine ( $T_4$ ), free thyroxine ( $FT_4$ ), or triiodothyronine ( $T_3$ ), in any of the three groups studied. These data indicate that hyperthyroidism is accompanied by normal plasma NE concentrations and that hypothyroidism is associated with significantly increased plasma NE concentrations, possibly in an attempt to compensate for the lack of thyroid hormones.

According to the above 7 clinical investigations including subjects with thyroid dysfunction and control group (N= 318)

6 indicators were investigated for the thyroid dysfunction:

Hands Delta SDC+ - SDC- : Increased in hyperthyroidism and decreased in hypothyroidism

SVR: Increased in hyperthyroidism and decreased in hypothyroidism

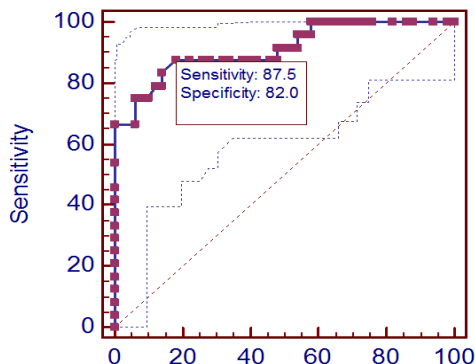
CO: Increased in hyperthyroidism and decreased in hypothyroidism

HR: Increased in hyperthyroidism and decreased in hypothyroidism

LF/HF: increased in hyperthyroidism and decreased in hypothyroidism

Norepinephrine: normal in hyperthyroidism and increased in hypothyroidism

Comparison of the Roc curves hypothyroidism /above indicators and final Roc curve including the 6 indicators



ROC curve		
Variable	Regression 6 indicators	
Classification variable	HYPOTHYROIDISM	
Sample size		318
Positive group :	diagnosis = 1	251
Negative group :	diagnosis = 0	67
Disease prevalence (%)		32.4
Area under the ROC curve (AUC)		0.911
Standard Error <sup>a</sup>		0.039
95% Confidence Interval <sup>a</sup>		0.822 to 0.965
z statistic		10.566
Significance level P (Area=0.5)		<0.0001