



Physiological Study on the Relation of Heart Rate Variability in Ageing and Thyroid Hormone Disorder

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ABSTRACT

The present study aimed to investigate whether cardiac autonomic dysfunction in aging human might be related to an underlying thyroid disturbance. ageing has been associated with hypothyroidism and cardiac autonomic dysfunction. On the basis of body mass index (BMI), 150 patients were grouped into three groups (n = 50) 48 years \pm 2, 55 years \pm 2 and 63 years \pm 2. Electrocardiogram was recorded using PowerLab system and the time and frequency domain measures of heart rate variability (HRV) were calculated. Fasting blood samples were drawn for measurement of serum thyroid stimulating hormone (TSH), total thyroxin (T4) and total triiodothyronine (T3) concentrations. The levels of TSH, T4 and T3 were not significantly different between the groups. The frequency domain HRV parameter reflecting parasympathetic tone (high-frequency normalized units, HFnu) was significantly reduced in aging third groups group. The parameters which reflect sympathetic activation (Heart rate, low-frequency normalized units; LFnu and the LF/HF ratio) were significantly increased in the aging group. HFnu was significantly and negatively correlated with age, whereas LFnu and LF/HF ratio were significantly and positively correlated with the above mentioned parameters. No significant relationships were noted between the HRV parameters and the levels of TSH or thyroid hormones. Cardiac autonomic dysfunction in aging human is not linked with underlying thyroid disturbance.

Key words: Heart rate variability, aging, Thyroid disturbance.

INTRODUCTION

Heart rate is mainly controlled by autonomic nerve activity to the sinoatrial node. Sympathetic and parasympathetic drive can be non-invasively investigated using Heart Rate Variability (HRV) analysis [8 & 9]. A low level of HRV associated with low vagal parasympathetic activity has been identified as a risk marker for all causes of mortality [8]. HRV can be altered by physiological factors, such as aging, gender and physical fitness. The aging process decreases HRV towards a lower parasympathetic modulation. [13 & 14]. Concerning gender, parasympathetic modulation of HRV seems to be generally higher in women than in men [8, 9, 17 & 18] however, aging tends to attenuate this difference [10, 11 & 12]. The change apparently beginning at the menopause [5]. The association between thyroid hormone and cardiac function is well established, and thyroid dysfunction, even mild, can significantly affect the cardiovascular system [6]. It has been shown that hyperthyroidism and hypothyroidism are both associated with sympathetic over activity and decreased vagal modulation of the heart rate [1, 2 & 3]. An elevated serum concentration of thyroid stimulating hormone (TSH), symptomatic of subclinical hypothyroidism, was commonly reported in human obesity [4]. Therefore, it is plausible to propose potential relationships between cardiovascular autonomic function and an underlying thyroid disturbance in young adult obese males. However, it's remained unknown whether cardiac autonomic dysfunction in young adult obese males might be related to an underlying thyroid disturbance or not. We, therefore, formulated the hypothesis that obese

young adult males, as compared with normal-weight counter- parts, will show cardiac autonomic dysfunction that is characterized by sympathetic dominance on the autonomic cardiovascular system, and that these differences would be associated with thyroid dysfunction. Heart rate variability (HRV), a measure of the continuous variations in heart rate, is a sensitive and non-invasive method that represents beat-to- beat control mechanisms mainly by the autonomic nerve supply to the sinoatrial (SA) node [8& 9]. Increased HRV has been recognized as a factor that indicates a healthy heart with quickly response of autonomic nervous system and SA node to internal or external environmental changes [7, 10, 11 & 12]. In contrast, a reduced HRV measures could reflect an altered sympathovagal balance of the SA node. This altered balance is characterized by a sympathetic activation and by a reduced vagal tone which has been strongly related to the pathophysiology of several diseases, including cardiovascular system diseases [19 & 20]. The risk for altered cardiac autonomic function is significant in overweight and obese subjects. Previous studies using HRV methods to measure cardiovascular autonomic function have indicated that obese individuals have a significant reduction in parasympathetic activity and a significant increase in sympathetic modulation of cardiac function, indicating a shift in the sympathovagal balance towards sympathetic predominance [22 & 23]. The aim of the present study was to identify the cardiac autonomic regulation in ageing human. 1HR: heart rate; SDNN: standard deviation of normal to normal intervals; RMSSD: root mean square of successive RR intervals difference; HFnu: high-frequency normalized units; LFnu: low-frequency normalized units; LF/HF: low frequency: high-frequency ratio; TSH: thyroid stimulating hormone; T4: thyroxin and T3: triiodothyronine in young and old human population.

MATERIALS AND METHODS

Blood samples

Blood samples were drawn from an antecubital vein into vacutainer tubes without anticoagulant in a sitting position. For serum collection, tubes were incubated in an upright position at room temperature for 15-30 min to allow clotting before centrifugation (10 minutes, 3000 rpm). Serum was immediately stored at -70°C until further analysis. Thyroid tests included TSH (normal rang 0.30-4.00 mIU/l), total thyroxin (T4; normal rang 4.4-11.6 $\mu\text{g/dl}$) and total triiodothyronine (T3; normal rang 0.69-2.02 ng/ml) were measured using commercial enzyme-linked immunosorbent assay kits (HUMAN Diagnostics, Wiesbaden, Germany).

Blood Pressure and HRV

Blood pressure was measured using mercury sphygmomanometers. ECG was digitally recorded in a quiet room (ambient temperature 22°C) with subjects lying in a supine position for 5 minutes using a biological amplifier (Bio Amp Model MLA2540, ADInstruments, Bella Vista, Australia) connected to a data acquisition system (Powerlab Model ML856, ADInstruments, Bella Vista, Australia). Standard time and frequency domain measures of HRV were calculated using HRV module LabChart 7.1 software (ADInstruments, Bella Vista, Australia). Time domain measures included heart rate, standard error of normal to normal intervals (SDNN) and the root mean square of successive RR intervals difference (RMSSD). Analysis of the power spectra was performed on two frequency ranges, revealing a Low frequency (LF) component between 0.05 and 0.15 Hz and a High frequency (HF) component between 0.15 and 0.40 Hz. The LF and HF measures were expressed in normalized units (LFnu and HFnu). The Low frequency: High frequency ratio (LF/HF), an estimate of sympathovagal balances in which a high ratio indicates greater sympathetic activity and a low ratio indicates greater parasympathetic activity, was also computed.

Statistical Analysis

All variables were reported as mean \pm standard error of mean (SEM). Data were analyzed using a one-way ANOVA followed by Duncan's post hoc test. Pearson's correlation coefficient was used to evaluate the correlations between the parameters of HRV and anthropometric measurements and between the measures of TSH, T3 and T4 and the parameters of HRV. All statistical analyses were performed with the SPSS statistical package version 15.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The mean values of age, hypertension, glucose, TSH and T3 & T4 levels in the three groups are presented in Table 1. The groups were different by age and significantly different were noted among groups for serum TSH, T4 and T3 concentrations ($p > 0.05$). As shown in Table 1. Also, there were significantly different in their blood glucose and hypertension in three groups according to age.

Table 1: Mean values of age, hypertension, glucose, TSH and T3 &T4 levels in the three groups

parameters	I (48 years)	II (58 years)	III (63 years)
Age	48 ± 0.41	58 ± 0.74	63 ± 0.82
Hypertension	152 ± 0.24	159 ± 0.26	160 ± 0.75
Glucose	7.31 ± 0.51	8.23 ± 0.63	9.54 ± 0.29
TSH (IU/ml)	1.8 ± 0.12	1.52 ± 0.56	1.45 ± 0.18
T3 (pmol/l)	1.62 ± 0.74	2.11 ± 0.21*	2.22 ± 0.36*
T4 (pmol/l)	12.22 ± 0.89	12.98 ± 0.85	13.11 ± 0.71*
Ratio T3/T4	0.13 ± 0.83	0.16 ± 0.24*	0.17 ± 0.51*

*Significantly different from normal-weight group, $p < 0.05$.

The present study showed that significant different between all parameters of heart rate; SDNN: standard deviation of normal to normal intervals; RMSSD: root mean square of successive RR intervals difference; HFnu: high-frequency normalized units; LFnu: low-frequency normalized units; LF/HF: low frequency/high-frequency ratio in group one and groups two and three. Also, there were significant different between group one and groups two and three in the heart rate, blood pressure systole and diastole as shown in table 2. The differences in HRV variables among the three groups. HF component, expressed in normalized units, was significantly higher in the second and third groups when compared with the first group. Also, the LF component was higher in the second and third groups when compared with the first group. Thus, the LF/HF ratio, which is thought to express the sympathetic and parasympathetic balance, was significantly higher in the second and third groups when compared with the first group indicated the sympathetic predominance over parasympathetic in these groups. Time domain HRV indices (i.e. SDNN and RMSSD) were only numerically higher in the second and third groups when compared with the first group. the heart rate was significantly higher in the second and third groups when compared with the first group as shown in Table 2.

Table 2: Mean values of heart rate, blood pressure and heart rate variability parameters in the three groups

parameters	I (48 years)	II (58 years)	III (63 years)
HR (bpm)	66.8 ± 2.0	66.2 ± 2.7	75.6 ± 2.9*
Blood pressure, systolic (mmHg)	152 ± 0.24	159 ± 0.26	160 ± 0.75
Blood pressure, diastolic (mmHg)	99.1 ± 0.25	100.2 ± 0.42*	103.3 ± 0.91*
SDNN (ms)	55.6 ± 0.18	59 ± 0.18	65.7 ± 0.14
RMSSD (ms)	62.3 ± 0.24	65.2 ± 0.54*	71.1 ± 0.82**
LFnu	45.5 ± 0.84	56.2 ± 0.92*	63.3 ± 0.44**
HFnu	62.6 ± 0.28	67.4 ± 0.43*	72.5 ± 0.12**
LF/HF	0.72 ± 0.14	0.83 ± 0.28	0.87 ± 0.47**

*Significantly different from normal-weight group, $p < 0.05$.

Table 3 shows the correlation between parameters of HRV and TSH and thyroid hormones. HFnu was significantly and negatively correlated in the second and third groups when compared with the first group, whereas LFnu and LF/HF ratio were significantly and positively correlated with the above mentioned parameters. No significant relationships were noted between any of the HRV variables and the thyroid hormones or TSH levels in the second and third groups when compared with the first group.

Table III. Correlation between parameters of heart rate variability and thyroid parameters in the three groups

Groups/ parameters	I (48 years)			II (58 years)			III (63 years)		
	TSH	T4	T3	TSH	T4	T3	TSH	T4	T3
HR (bpm)	0.093	0.049	0.048	0.123	0.059	0.058	0.159	0.055	0.061
SDNN	0.043	0.344	0.036	-0.051	-0.357	-0.052	-0.074	-0.355	-0.054
RMSSD	0.04	0.241	0.122	-0.05	-0.255	-0.133	-0.06	-0.266	-0.152
LFnu	0.031	0.039	0.075	-0.035	0.040	-0.080	-0.038	0.043	-0.083
HFnu	0.005	0.073	0.152	0.006	0.080	0.164	0.007	0.081	0.170
LF/HF	0.021	0.058	0.155	0.022	0.061	0.165	0.025	0.065	0.172

DISCUSSION

Thyroid disease is common in the general population and the prevalence increases with age [15]. Hypothyroidism is the most common thyroid disorder in the adult population, especially in older women. It is usually autoimmune in origin, presenting as either primary atrophic hypothyroidism or Hashimoto's thyroiditis [16]. The aim of the present study was to identify the cardiac autonomic regulation in ageing human. ¹HR: heart rate; SDNN: standard deviation of normal to normal intervals; RMSSD: root mean square of successive RR intervals difference; HFnu: high-frequency normalized units; LFnu: low-frequency normalized units; LF/HF: low frequency: high-frequency ratio; TSH: thyroid stimulating hormone; T4: thyroxine and T3: triiodothyronine. Several authors have

observed normal, reduced or elevated thyroid hormones and TSH baseline concentrations in adult individuals [21, 8 & 9]. The mean serum levels of TSH, as well as the levels of thyroid hormones (TT3 and TT4) were not significantly different between the groups in this study. also, there were observed different between circulating TSH and thyroid hormone levels and the body compositions. Significantly higher in the second and third groups when compared with the first group indicated the sympathetic predominance over parasympathetic in these groups. TSH: thyroid stimulating hormone; T4: thyroxin; T3: triiodothyronine; Significantly higher in the second and third groups when compared with the first group TSH: thyroid stimulating hormone; T4: thyroxin; T3: triiodothyronine to examine relationships between cardiac autonomic function and the thyroid status. Our main findings were: an increase in age was accompanied with increase in heart rate and low HRV indicating an increased sympathetic and a reduced vagal modulation of sinus node. Thyroid parameters and the cardiac autonomic dysfunction which observed in age human population. Power spectrum analysis of HRV can estimate the state of sympathovagal balance modulating SA node activity [8 & 9]. In addition to the RR interval, the normalized powers of the LF and HF components (LFnu and HFnu) of the HRV appear to be the most sensitive markers on an individual basis for sympathetic and vagal modulations, respectively [8 & 9]. As well, higher values of LF/HF ratio indicate a more sympathetically driven cardiovascular system [24, 8 & 9]. In the current study it was shown that the LF/HF ratio, in addition to the LFnu component, was higher in the second and third groups when compared with the first group, indicating a shift in the sympathovagal balance toward an increment in sympathetic activation. Further, results of the present study show a lower parasympathetic activity in the second and third groups when compared with the first group as reflected by a significantly lower HFnu component. Obviously, sympathetic activation and diminished parasympathetic nervous system activity results in heart rate acceleration the second and third groups when compared with the first group. These results are in keeping with the results of previous investigators who found that obesity is related to sympathovagal imbalance characterized by depressed parasympathetic tone and increased sympathetic activity [25, 26, 27, 8 & 9]. Interestingly, their differences were observed in HRV indices in the second and third groups when compared with the first group. This finding expresses the fact that progression from young adult human is associated with changes in autonomic regulation of the cardiovascular system in the second and third groups when compared with the first group. Our finding is in agreement with that of [18], who observed no differences in HRV measures between the children and age. Researchers have reported significant improvement in autonomic cardiac modulation through a shift toward greater vagal tone with diet-induced weight loss and exercise [28, 29 & 32]. Therefore, interventions to increase HRV in overweight subjects, such as exercise therapy or dieting, may enhance vagal tone and thereby decrease their susceptibility to cardiac autonomic dysfunction. Our findings are in agreement with [33 & 31], who found no difference in serum TSH between euthyroid obese subjects and the control group. Our findings are also consistent with the previous observations of [29 & 30], who described no associations between TSH and body composition among euthyroid young men. However, in contrast, other authors found that in euthyroid adults without a history of thyroid disease, In our study, all subjects were actually in a euthyroid state as the concentrations of TSH, T3 and T4 were within the normal range in all groups. This might be a potential elucidation for the lack of associations between TSH and the parameters of body compositions in this study as the associations with TSH in other studies can be caused by subclinical thyroid dysfunction [30]. Additionally, the lack of associations between thyroid hormones and age can be explained by that peripheral tissue metabolism of thyroid hormones was affected by age [10 & 11]. Similarly with our observations for body composition, all the measured HRV variables were correlated with the TSH, T3 and T4 levels. Therefore, it is evident from the present study that alteration in the cardiovascular autonomic function in the second and third groups when compared with the first group was linked to the levels of thyroid hormones and TSH. However, hypothyroidism and hyperthyroidism have been associated with sympathetic over activity on the autonomic cardiovascular system [8 & 9]. The present study illustrate a relationship between cardiac autonomic dysfunction and thyroid profile in age human population, the association of age and a shift in cardiac sympathovagal balance towards a more sympathetic state older human. One can hypothesize that age might be associated with increases in many hormonal and metabolic parameters that may cause increased sympathetic activity and decreased parasympathetic activity. For example insulin resistance, elevated catecholamine levels and the degree of hyperlipidemia have also been proposed as potential mechanisms underlying the association between ageing human and cardiac autonomic dysfunction [19, 8 & 9].

The aim of the present study was to identify the cardiac autonomic regulation in ageing human. 1HR: heart rate; SDNN: standard deviation of normal to normal intervals; RMSSD: root mean square of successive RR intervals difference; HFnu: high-frequency normalized units; LFnu: low-frequency normalized units; LF/HF: low frequency: high-frequency ratio; TSH: thyroid stimulating hormone; T4: thyroxin and T3: triiodothyronine in young and old human population.

CONCLUSION

We conclude that alteration of thyroid hormones is a common feature in aging. Further study is needed to compare thyroid hormone levels and present study was to identify the cardiac autonomic regulation in ageing human. 1HR: heart rate; SDNN: standard deviation of normal to normal intervals; RMSSD: root mean square of successive RR intervals difference; HFnu: high-frequency normalized units; LFnu: low-frequency normalized units; LF/HF: low frequency: high-frequency ratio; TSH: thyroid stimulating hormone; T4: thyroxin and T3: triiodothyronine in young and old human population. This study showed that the above parameters were significantly higher in the second and third groups when compared with the first group indicated the sympathetic predominance over parasympathetic in these groups.

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