BALNEO RESEARCH Balneo and PRM Research Journal
English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

Research article

Heart rate variability and anthropometric parameters in smoker's vs nonsmoker's status

Daniela-Viorelia Matei [1], Catalina Luca [1,*], Dan Trofin [1], Robert Fuior [7], Ilie Onu [1,*], Cristiana Onita [2], Madalina Datcu [3,4], Oana-Diana Hrisca-Eva [1]

Citation: Matei D.V., Luca C., Trofin D., Fuior R. , Onu I., Onita C., Datcu M., Hrisca-Eva O.D. - Heart rate variability and anthropometric parameters in smoker's vs nonsmoker's status *Balneo and PRM Research Journal* ***2024**, 15(1): 658*

Academic Editor(s):
Constantin Munteanu

Reviewer Officer:
Viorela Bembea

Production Officer:
Camil Filimon

Received: 06.02.2024
Published:31.03.2024

Reviewers:
Liliana Stanciu
Corina Sporea

Publisher's Note: Balneo and PRM Research Journal stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1 Grigore T. Popa University of Medicine and Pharmacy Iasi, Faculty of Medical Bioengineering, Department of Biomedical Sciences, daniela.matei@umfiasi.ro, catalina.luca@umfiasi.ro, ilie.onu@umfiasi.ro, robert.fuior@umfiasi.ro, oana.hrisca@umfiasi.ro, manolachecristiana@yahoo.com, dan.trofin@umfiasi.ro
2 Grigore T. Popa University of Medicine and Pharmacy Iasi, Faculty of Medicine, Department of Fisiophatology, manolachecristiana@yahoo.com
3 Technical University Gheorghe Asachi Iasi, Faculty of Electrical Engineerig, madalina.dtc@gmail.com
4 4Grigore T. Popa University of Medicine and Pharmacy Iasi, Faculty of Medicine, Department of Medical Informatics and Biostatistics, madalina.dtc@gmail.com

* Correspondence: Catalina LUCA catalina.luca@umfiasi.ro; Ilie Onu ilie.onu@umfiasi.ro

Abstract: Heart rate variability (HRV) is a simple way to explore autonomic nervous activity. Current studies emphasize the need to identify a dependent relationship between smoking habit and HRV. The findings of these studies could demonstrate that smoking can have both an acute and a chronic effect on HRV. The aim of this study is to investigate the relationship between smoking and anthropometric data such as body weight, body fat distribution and heart rate variability. Our study involves measuring HRV parameters at rest and during two tests that are part of the Ewing test battery. Through the obtained data we can demonstrate that active smoking is associated with a reduction in HRV. At the same time, we can state that HRV is affected by different behavior patterns of the smoker.complex individualized rehabilitation treatment.

Keywords: Heart rate variability; anthropometric parameters; active smoking

1. Introduction

Smoking stands as a formidable challenge to public health, with staggering statistics revealing that over 8 million individuals succumb prematurely to tobacco addiction annually. Among these, 7 million fall victim to the direct consequences of tobacco consumption, while a substantial 1.2 million, who have never smoked, face indirect repercussions [1].

Recent research underscores the multifaceted impact of smoking, indicating a heightened risk of abdominal obesity, the onset of metabolic irregularities, cardiovascular diseases, and an increased susceptibility to cancer development [2-6]. Notably, studies reveal that central obesity in young men emerges as a primary consequence of active smoking, influencing parameters such as body mass index (BMI) and waist circumference (WC) [7].

The intricate web of health implications extends to the autonomic nervous system, particularly explored through heart rate variability (HRV). HRV serves as a simple yet insightful method to gauge the modulation of sympathetic and parasympathetic activity. Reduced HRV has been identified as an indicator of overall health deterioration, correlating with heightened sympathetic or diminished vagal tone, potentially predisposing individuals to a higher risk of arrhythmias and sudden cardiac death [8-10]. Ongoing studies are fervently delving into the intricate relationship between smoking habits and HRV, aiming to establish a connection that spans both acute and chronic effects of smoking on HRV [11, 12].

This study endeavors to unravel the intricate interplay between smoking, body weight, body fat distribution, and heart rate variability. The investigation encompasses the measurement of these parameters both at rest and during two specific tests integral to the Ewing test battery – the deep breathing and standing tests [13]. By scrutinizing these facets, the research aims to contribute valuable insights into the comprehensive impact of smoking on physiological well-being and lay the groundwork for more effective public health interventions.

2. Subjects and methods

2.1. Participant recruitment and inclusion criteria

40 smoking students (with an average age of 20.512 ± 1.121 years; 22 women and 18 men) and 40 never-smokers' students (age 20.22 ± 0.49 years; 20 women and 20 men) from the Faculty of Medical Bioengineering, University of Medicine and Pharmacy Grigore T. Popa Iasi were part of our study.

The study was approved by our institutional ethics committee registration number 31/15.01.2021 and all the patients gave consent in accordance with ethical principles. The study was carried out in accordance with the Helsinki Declaration.

Smoking status was divided into two categories: current and never. Smoking status was assessed with a single question ("Do you smoke?") with dichotomous response format (yes/no).

All subjects completed the stress perception scale, which is a self-administered questionnaire that explores the subjective feeling of stress compared to last month. It has 14 items on a scale from 1 - Never to 5 - Often. A total perceived stress score is calculated that can vary between 14 and 70, where high scores indicate a higher level of stress [14].

The inclusion criteria were as follows: age between 20 and 25 years, smoker, or non-smoker, with normal clinical evaluation and a normal electrocardiographic evaluation in the last 3 months.

Subjects diagnosed with cardiovascular disease, those who demonstrated an arrhythmia during the current evaluation, subjects with metabolic pathology, subjects with medication that influence heart rate (beta-blocking medication), with fever or hypoxia were excluded from the study.

2.2. Clinical and paraclinical assessment

In the study, an important parameter is that of anthropometric data. These data included measurement of height, weight, body mass index (BMI) and waist circumference (WC). The study protocol involved the measurement of height in m and body weight in kg, using a digital scale. The subject was asked to wear light clothing and the data was recorded with the subject barefoot. Waist circumference was also measured. With the subject standing, waist circumference was measured with a waist measuring tape. Landmarks were taken from the lower costal margin and iliac crest, in front of end expiration. Waist circumference was measured twice and the average of the two measurements was used for analysis. WC is an important indicator of visceral fat. WC has the value of 94 centimeters or more for men and 80 centimeters or more for women. Elevated values occur in patients at high risk of type 2 diabetes, dyslipidemia, hypertension, and cardiovascular disease [15].

Total body fat, muscle mass, body water, visceral fat, subcutaneous fat, bone mass, were evaluated using "Health U" of the ACEVIVI intelligent scale, a bio-electric impedance technology. Bio-impedance analysis determines the weight of different compartments (fatty tissue, non-fatty water, intra and extracellular) based on different electrical conductivities of tissues (non-fat tissue - conductor and fatty tissue - resistant to micro-current passage) [15]. This information is then processed by the embedded software.

The methods with the highest accuracy in determining total body fat, visceral fat and subcutaneous cell tissue are computed tomography, nuclear magnetic resonance and dual X-ray absorption, methods extremely difficult to apply in current medical practice.

Body mass index (kg / m2) was calculated as weight divided by the square height. BMI classifications are underweight (under 18.5 kg / m2), normal weight (18.5-24.9), overweight (25-29.9) and obese (30 or more). BMI below 20 in those over 25 years of age has been associated with higher mortality [16].

Systolic and diastolic blood pressure (SBP and DBP) were measured in supine position and upright using an aneroid cuff sphygmomanometer with an adult cuff. Blood pressure was measured twice in a row in the right arm of the seated participant after sitting quietly for 5 minutes. The average of these two measurements was used for analysis. Blood pressures were measured upright. Orthostatic hypotension was defined as a 20 mmHg decrease in TAP or a 10 mmHg decrease in TAP within three minutes of standing compared to lying blood pressure. Pulse pressure, measured as the difference between maximum SBP and DBP, was calculated. Hypertension was defined as an SBP greater than 140 mmHg or a DBP greater than 90 mmHg or both.

2.3. Measurement of heart rate variability

Using the BIOPAC®Acquisition System and AcqKnowledge software, version 3.9.1.6., an electrocardiogram for a period of 10 minutes at rest was recorded, for all the subjects in study.

Tests were performed between 4-6 PM, after 30 minutes of resting position in supine position, at a temperature of 22^{o}C, in a quiet room, without prior physical effort or ingestion of caffeinated or alcoholic beverages 24 hours before the evaluation.

The ECG recording was then corrected for abnormal artifacts and beats, then the signal was analyzed using Kubios analysis software version 2.2 (Biosignal Analysis and Medical Imaging Group, University of Eastern Finland.

The time domain of the HRV parameters were analyze such as media RR, standard deviation of the normal intervals NN –SDNN, the square root of the mean differences of the successive normal intervals (NN) –RMSSD and the NN intervals longer than 50 ms - pNN50 [17]. The time domain analysis parameters, i.e., SDNN, RMSSD, are thought to reflect the activities of the parasympathetic nervous system.

The frequency domain parameters analyzed were high frequency (HF) from 0.15 to 0.4 Hz (characteristic to parasympathetic activity), low frequency (LF) from 0.04 to 0.15 Hz (characteristic to both sympathetic and parasympathetic activation), normalized LF, normalized HF and LF / HF ratio were measured [17].

We then monitored HRV during 2 Ewing tests (heart rate during 10 minutes of deep breathing and heart rate change after 10 minutes of standing). The test sequence was standardized: resting state, deep breathing test and standing tests for all students enrolled in our study.

The evaluation technique using the 2 Ewing tests has been described in other studies [18]. The "deep breath test" was used to assess parasympathetic functions and the "permanent test" was used to assess sympathetic functions [13].

2.4. Statistical analysis

For data analysis, he used the Statistical Package for the Social Sciences software V.24. (IBM Statistical Package for the Social Sciences, Chicago, Illinois). The normal distribution of the data was also tested ($p<0.05$) using the Shapiro - Wilk test. Mean and standard deviation were calculated for all variables. Pearson Correlation was determined for measuring the correlation between two sets of data. The Independent "t Student" test was performed to see if there is a statistically significant difference between HRV parameters for smokers and non-smokers groups.

The relationship between AGV, body fat mass, anthropometric, clinical, biochemical parameters and personal history was assessed by correlation analysis. The applied correlation coefficients were different in relation to the shape of the data distribution: Pearson (r), when both variables were numerical and normally distributed and the

Spearman coefficient (ϱ) when one of the two variables was nominal or had a distribution that showed significant deviations of to normal distribution.

3. Discussion

The students were divided into 2 groups as follows: never-smokers group (N=40) and smokers' group (N=40). The anthropometric and clinical data of subjects are shown in Table I.

Table 1. Anthropometric and clinical features of the groups

Parameter	Never Smokers N=40	Smokers N=40	p
Age (years)	20.300 ± 0.563	20.500 ± 1.154	0.332
Stress	38.450 ± 6.353	41.475 ± 6.068	0.032
Height (cm)	171.450 ± 8.047	165.320 ± 28.140	0.426
Weight (kg)	64.220 ± 13.057	69.957 ± 16.257	0.061
BMI (kg/m^2)	22.16 ± 4.189	23.682 ± 3.739	0.090
Body fat	21.461 ± 7.144	24.667 ± 7.399	0.066
Muscle mass	45.280 ± 7.832	47.265 ± 10.515	0.341
Body water	52.192 ± 5.295	49.355 ± 5.125	0.017
Visceral fat	4.032 ± 2.983	5.558 ± 3.187	0.040
Bone mass	2.665 ± 0.320	2.762 ± 0.459	0.273
Subcutaneous fat	14.365 ± 5.036	17.408 ± 5.032	0.008
Waist circumference (cm)	73.350 ± 10.445	79.500 ± 12.878	0.014
Hip circumference (cm)	94.750 ± 9.009	98.650 ± 10.326	0.075
SBP supine (mmHg)	115.129 ± 9.657	121.000 ± 10.268	0.015
DBP supine (mmHg)	70.935 ± 5.477	72.674 ± 6.913	0.249
PP supine (mmHg)	44.065 ± 8.880	48.256 ± 9.325	0.055
SBP upright (mmHg)	113.032 ± 10.892	119.698 ± 12.349	0.018
DBP upright (mmHg)	78.032 ± 10.499	82.326 ± 8.665	0.058
PP upright (mmHg)	35.065 ± 9.757	37.651 ± 11.237	0.305
Age (years)	20.300 ± 0.563	20.500 ± 1.154	0.332

BMI—body mass index, SBP—systolic blood pressure, DBP — diastolic blood pressure, PP- pulse pressure. Data: expressed as mean ± standard deviation.

The age, height, weight, BMI, body fat, muscle mass, bone mass and hip circumference were not different between the groups. But visceral fat ($p<0.040$), subcutaneous fat ($p<0.008$) and waist circumference ($p<0.014$) were increased, with statistical significance, in smoker group when we compare with never-smoker group (Table I).

Smokers presented higher SBP values in supine and upstanding condition compared to non-smokers. After the analysis, it was found that there was no significant difference between the groups for DBP in the supine position. But an increased value for DBP was recorded during the orthostatic test, as can be seen in the Table. Pulse pressure also suffered a significant increase in smokers ($p<0.05$).

Time-domain and frequency parameters of HRV in resting state can be observed in Table II. HRV parameters in resting state presented a decreased vagal modulation, reflected by lower values of RMSSD ($p<0.027$), pNN50 ($p<0.013$), HFnu ($p<0.004$) in smokers compare with never-smokers (Table II).

Table 2. HRV parameters in resting state

HRV parameters in deep breathing test	Never Smokers N=40	Smokers N=40	Levene test	P Independent t test
RR (ms)	700.98 ± 117.59	653.39 ±74.86	0.012	0.034
SDNN	51.95 ± 24.33	42.41 ± 16.74	0.036	0.044
HR (b/min)	84.79 ± 11.90	93.37 ± 10.41	0.045	0.001
STD HR	6.19 ± 2.91	5.88 ± 1.73	0.054	0.571
RMSSD (ms)	54.41 ± 35.52	39.77 ± 20.62	0.036	0.027
pNN50	18.89 ± 16.51	10.83 ± 11.34	0.000	0.013
VLF (ms^2)	109.15 ± 87.33	88.93 ± 87.77	0.243	0.304
LF (ms^2)	1458.30 ± 1242.86	1126 ± 962.34	0.255	0.185
HF (ms^2)	1274.3 ±1213.67	718.75 ±675.24	0.003	0.013
LF nu	55.35 ± 13.42	62.86 ± 11.79	0.554	0.009
HF nu	44.11 ± 13.54	35.94 ± 10.79	0.110	0.004
LF/HF	1.319 ± 0.731	2.022 ± 1.292	0.018	0.003

SDNN — standard deviation of all NN intervals, RMSSD — square root of the mean of the sum of the squares of differences between adjacent NN intervals, pNN50% — percentage of differences between adjacent NN intervals differing more than 50 ms, VLF- very low frequency, LH — low frequency component, and HF — high frequency component. Data: expressed as mean ± standard deviation; p-value < 0.05 was considered to be statistically significant

Mean heart rate (HR) beat/minute was increased among smokers (93.37 ± 10.41 beat/min) when compare with never smokers (84.79 ± 11.90), with p<0.001. Also, LF/HF increased in smokers 2.022 ± 1.292 vs 1.319 ± 0.731 never smokers, p<0.003.

A reduction in parasympathetic activity was observed in smokers especially during the deep breathing test, as can be seen in Table III. For differentiation, HFnu (expressed in normalized units) was used, which is unanimously considered a marker of parasympathetic activity. In the case of our subjects, HF was 29.62 ± 10.71 in smokers vs 34.79 ± 10.41 in non-smokers, with p<0.031. In this situation we can appreciate the fact that a lower HF value indicates a diminished vagal influence on the heart rate. So we can state that smokers have a reduced heart rate variability. Increased LF/HF ratio in smokers 2.77 ± 1.29 vs 1.90 ± 0.99 never smokers (p<0.001) is correlated with reduced vagal influence and increased sympathetic control of heart rate as can be seen in Table III.

Table 3. HRV parameters in deep breathing test

HRV parameters in deep breathing test	Never Smokers N=40	Smokers N=40	Levene test	P Independent t test
RR (ms)	696.21 ± 89.49	654.36 ± 73.10	0.359	0.025
SDNN	95.198 ± 32.20	81.98 ± 29.11	0.168	0.057
HR (b/min)	89.42 ± 11.27	94.28 ± 10.00	0.350	0.044
STD HR	12.15 ± 2.91	10.18 ± 3.36	0.266	0.006
RMSSD (ms)	86.98 ± 33.74	64.53 ± 32.04	0.344	0.003
pNN50	20.35 ± 11.61	14.86 ± 9.74	0.256	0.024
VLF (ms^2)	221 ± 177.32	161.05 ± 134.39	0.054	0.092
LF (ms^2)	5929.90 ± 5124.64	5910.30 ± 4819.19	0.088	0.362
HF (ms^2)	2533.27 ± 2458.80	1995.02 ± 1669.65	0.097	0.255
LF nu	64.73 ± 10.56	70.57 ± 10.69	0.762	0.016
HF nu	34.79 ± 10.41	29.62 ± 10.71	0.847	0.031
LF/HF	1.90 ± 0.99	2.77 ± 1.29	0.076	0.001

SDNN — standard deviation of all NN intervals, RMSSD — square root of the mean of the sum of the squares of differences between adjacent NN intervals, pNN50% — percentage of differences between adjacent NN intervals differing more than 50 ms, VLF- very low frequency, LH — low frequency component, and HF — high frequency component. Data: expressed as mean ± standard deviation; p-value < 0.05 was considered to be statistically significant

The sympathetic activation test led to a more pronounced sympathetic response in both groups of students, with not statistical difference between them (Table IV).

Using Pearson correlation analysis, the stress test was correlated with HR (r= 0.61, p<0.007), and negatively correlated to RMSSD (r= -0.40, p<0.008), pNN50 (r= -0.42, p<0.005). BMI was correlated with LF/HF (r=0.31, p<0.05) and HF (r= -0.31, p<0.05). Visceral fat was direct correlated with LF nu (r=0.43, p<0.005), LF/HF (r=0.44, p<0.003) and negatively with RMSSD (r= -0.38, P<0.01), HF nu (r= -0.46, p<0.002).

Table 4. HRV parameters in in standing test

HRV parameters in deep breathing test	Never Smokers N=40	Smokers N=40	Levene test	P Independent t test
RR (ms)	640.02 ± 96.00	603.82 ± 72.85	0.024	0.061
SDNN	52.58 ± 35.02	51.36 ± 29.65	0.666	0.867
HR (b/min)	96.61 ± 14.54	101.16 ± 11.63	0.150	0.127
STD HR	7.85 ± 3.52	7.57 ± 3.56	0.966	0.730
RMSSD (ms)	49.88 ±47.18	50.33 ± 34.91	0.481	0.962
pNN50	10.49 ± 12.08	7.19 ± 8.61	0.040	0.163
VLF (ms^2)	146.17 ± 145.02	148.30 ± 79.05	0.063	0.935
LF (ms^2)	1663.27 ± 1441.72	1443.12± 1414.07	0.246	0.490
HF (ms^2)	917.85 ± 868.95	916.45 ± 798.21	0.220	0.848
LF nu	68.26 ± 14.24	64.44 ± 13.01	0.001	0.214
HF nu	31.34 ± 14.23	35.41 ± 12.91	0.998	0.185
LF/HF	2.88 ± 2.32	2.25 ± 1.32	0.053	0.136

SDNN — standard deviation of all NN intervals, RMSSD — square root of the mean of the sum of the squares of differences between adjacent NN intervals, pNN50% — percentage of differences between adjacent NN intervals differing more than 50 ms, VLF- very low frequency, LH — low frequency component, and HF — high frequency component. Data: expressed as mean ± standard deviation; p-value < 0.05 was considered to be statistically significant

5. Discussion

The present study succeeded in demonstrating that smoking, in addition to increasing sympathetic activities, led to an increase in abdominal and visceral fat in smokers.

According to the analyzed data, we can conclude that smokers, although they have a normal BMI, have a much larger amount of adipose tissue compared to those who never smoke. These conclusions are supported by multiple studies that have suggested that smoking is associated with abdominal obesity in smokers even though they have a normal BMI [19 - 21].

The implications of reduced heart rate variability (HRV) in smokers carry significant consequences for their long-term health. HRV, reflecting the autonomic nervous system's balance, plays a crucial role in maintaining cardiovascular health and overall well-being. When HRV is diminished, especially in the context of smoking, several adverse effects may unfold:

- Increased Risk of Arrhythmias: Reduced HRV is associated with an elevated risk of arrhythmias. Smoking-induced alterations in autonomic balance can disrupt the heart's electrical signaling system, leading to irregular heartbeats. Persistent exposure to these conditions may contribute to the development of more severe arrhythmias over time.
- Sudden Cardiac Death: Diminished HRV has been linked to an increased risk of sudden cardiac death. Smokers with reduced HRV may face a higher likelihood of experiencing life-threatening cardiac events, posing a substantial long-term health risk.
- Cardiovascular Diseases: Smoking is a well-established risk factor for cardiovascular diseases (CVD), and reduced HRV further compounds this risk.

The compromised autonomic balance may contribute to the progression of atherosclerosis, hypertension, and other cardiovascular conditions, potentially leading to more severe and earlier onset of CVD in smokers.

- Impaired Stress Response: HRV is intricately connected to the body's ability to respond to stress. Smokers with reduced HRV may exhibit impaired stress resilience, affecting their overall ability to cope with daily challenges. Chronic stress has its own set of health implications, including mental health disorders and an increased risk of cardiovascular events.
- Compromised Exercise Tolerance: HRV influences the body's response to physical exertion, and reduced HRV in smokers may translate into compromised exercise tolerance. This limitation can contribute to a sedentary lifestyle, further exacerbating the risk of obesity and related health issues.
- Delayed Recovery from Illness: HRV is considered a marker of general health and resilience. Smokers with reduced HRV may experience delayed recovery from illnesses due to compromised autonomic function, potentially leading to prolonged periods of morbidity.

Understanding the long-term health effects of reduced HRV in smokers highlights the intricate connection between tobacco use and cardiovascular health. Smoking cessation efforts and interventions aimed at improving HRV may prove pivotal in mitigating these risks, promoting overall health, and preventing the progression of cardiovascular diseases in this population.

The focus point of this study is the stability of a relationship between smoking, stress and changes in HRV. We found that smokers had a higher perception of stress. From here we can say that smokers have a lower body weight because they eat less when they are stressed.

Significant decrease in RMSSD and HF indicates parasympathetic dysfunction. It also increases LF and LF / HF demonstrates a dysfunction of the autonomic nervous system with sympathetic predominance. Smokers with a high level of stress have an imbalance between PNS activity and SNS activity, which was revealed in our study. Several clinical studies show that HRV levels are lower in heavy smokers than in non-smokers [22 - 24].

Nicotine, as the main addictive compound of tobacco smokers seems to be the main disruptive factor on the autonomic nervous system [25]. It immediately enters the bloodstream through the lungs and oral mucosa. From here it attaches to the central nervous system at the level of acetylcholine receptors and causes an increase in the concentration of norepinephrine in the nucleus accumbens and locus coeruleus. In this situation it is practically provoked or sensation of psycho-intellectual stimulation. ANS dysfunction has also been found to be primarily caused by nicotine, as it affects the functions of carotid body chemoreceptors and aortic baroreceptors. In this way, peripheral nicotinic acetylcholine receptors are desensitized, which play a mediating role in the transmission of the autonomic ganglion [25].

Our findings suggest that smoking is accompanied by a marked and prolonged increase in heart rate and blood pressure, along with increased activity of the sympathetic system that may contribute over time to cardiovascular damage. A recent study showed an increase in the intima-media thickness of the carotid artery in adolescents who currently smoke [26].

Body weight is under the control of ANS which regulates insulin and leptin. Leptin decreases secretions and inhibits the actions of insulin. Insulin is the most powerful antilipolytic hormone, regulating anabolic actions on adipose tissue, stimulates the absorption of glucose and free fatty acids, inhibits lipolysis, promotes re-esterification of fatty acids into triglycerides and stimulates lipogenesis [27].

Leptin is a hormone produced mainly by adipose tissue that acts on specific receptors in the hypothalamus to reduce appetite. Leptin exerts all the effect on the cardiovascular level through sympathetic activation such as: vascular functional regulation, amplification of platelet aggregation and inefficient fibrinolysis, angiogenesis, thus being involved in the pathogenesis of cardiovascular disease [28].

Leptin secretion is increased by insulin, corticosteroids, TNF-alpha and estrogen and is decreased by androgens, growth hormones, catecholamine, free fatty acids [29]. Leptin promotes weight loss by increasing energy expenditure by stimulating the NHS in the thermogenic brown fat country and in non-thermogenic organs (heart, kidneys, adrenal medulla). Leptin stimulates the generation of endothelin by endothelial cells that can underlie endothelial dysfunction in metabolic syndrome and type 2 diabetes. Obesity, insulin resistance and a reduced glucose tolerance can be caused by leptin deficiency [30]. Weight loss reduces leptin levels and increases insulin sensitivity. One of the indirect effects of increased catecholamine levels in smokers appears to be related to lower leptin levels [31].

Nicotine has been shown to increase blood pressure and heart rate [32] and can induce endothelial dysfunction by inhibiting the activation of endothelial synthetic nitric oxide (eNOS) and decreasing the generation and bioavailability of nitric oxide (NO) [33]. A recent study showed that nicotine up-regulates CD36 expression in monocytes / macrophages by facilitating the encapsulation of lipid particles by macrophages [34]. Nicotine-stimulated macrophages secrete increased inflammatory cytokines, resulting in an inflammatory process in the sub endothelium [35].

Smoking cessation and smoking cessation should be promoted among young people to prevent the occurrence of autonomic dysfunctions, obesity, and associated complications.

There are studies that show that lifestyle changes by quitting smoking, restricted diets, physical training programs, stress reduction techniques can use the functions of ANS. For example, increased parasympathetic activity and decreased sympathetic activity occurs after weight loss, dieting, and exercise. Weight gain and lack of exercise have the opposite effect. Hart et al. showed that participants who successfully quit smoking, compared to those who did not, demonstrated an increase in HRV indicators [36].

A possible limitation of our study is the presence of a small number of subjects. This decreases the statistical power in detecting differences between groups, thus not allowing us to generalize the results. These results should be confirmed in larger studies that specifically address the relationship between smoking, adipose tissue, and autonomic functions. Using self-reporting tools to diagnose stress was another drawback. Another limitation is that we did not measure plasma nicotine or epinephrine levels and did not correlate them with autonomic changes. Also, in this study, basic activities of the parasympathetic and sympathetic systems were studied, excluding the acute effects of smoking.

The autonomic balance measured by HRV is not usually assessed in daily practice, but HRV could be a useful tool to assess and prevent autonomic nervous system dysfunction and thus future cardiovascular damage in young people.

6. Conclusions

In conclusion, active smoking is associated with a reduction in HRV, as evidenced by a reduction in parasympathetic activity indicators. At the same time, we can state that HRV is affected by the different behavior patterns of the smoker. For much more accurate results we propose to include in the future subjects with different behaviors regarding smoking, such as active smoking considering the history and intensity of smoking, with the possibility of extending to exposure to passive smoking, to be able to establish exactly which it is the relationship between smoking and HRV on a temporal scale.

Author Contributions: All the authors have the same contribution. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Grigore T. Popa University of Medicine and Pharmacy Iasi (31/15.01.2021).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data are contained within the main text of the article. Raw data were generated at Faculty of Physical Education and Sports, University of Craiova. Derived data supporting the findings of this study are available from the corresponding author C.L. and I.O. on request.

Acknowledgments: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. WHO - Fact Sheet: Tobacco, 27 May 2020
2. Canoy D, Wareham N, Luben R, Welch A, Bingham S, et al. Cigarette smoking and fat distribution in 21,828 British men and women: a population-based study. *Obes Res* **2005**, *13*: 1466–1475.
3. Kim JH, Shim KW, Yoon YS, Lee SY, Kim SS, et al. Cigarette Smoking Increases Abdominal and Visceral Obesity but Not Overall Fatness: An Observational Study. *PLoS ONE* **2012**; *7:* e45815
4. Sairenchi T, Iso H, Nishimura A, Hosoda T, Irie F, et al. Cigarette smoking and risk of type 2 diabetes mellitus among middle-aged and elderly Japanese men and women. *Am J Epidemiol* **2004**; *160*: 158–162.
5. Goldman J, Klinger M. Effect of smoking on the course of essential hypertension: a follow-up study of a group composed predominantly of women. *Med Sci Monit* **2001**; *7*:1280–1284.
6. Sopori M. Effects of cigarette smoke on the immune system. *Nature Reviews Immunology* **2002**; *2*(5):372-377.
7. Su P, Hong L, Sun H, Zhao YF, Li L. Age plays an important role in the relationship between smoking status and obesity risk: a large-scale cross-sectional study of Chinese adults. *Int J Clin Exp Med*. **2015**; *8*(10):18894-18906.
8. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *Circulation* **1996**; *93*:1043–1065
9. Stein PK, Fauchier L, Babuty D. Sudden death, arrhythmic events, and measurements of heart rate variability. *J Am Coll Cardiol* **1999**; *34*(7):2148–9.
10. Thayer JF, Yamamoto SS, Brosschot JF. The relationship between autonomic imbalance, heart rate variability and cardiovascular disease risk factors. *Int J Cardiol* **2010**; *141* (2):122–31.
11. Girard D, Delgado-Eckert E, Schaffner E, Ha¨cki C, Adam M, Stern GL, et al. Long-term smoking cessation and heart rate dynamics in an aging healthy cohort: Is it possible to fully recover? *Environ. Res.* **2015**; *143*:39–48.
12. Dinas PC, Koutedakis Y, Flouris AD. Effects of active and passive tobacco cigarette smoking on heart rate variability. *Int J Cardiol.* **2013**; *163*(2):109–15.
13. Ewing DJ, Clarke BF Autonomic neuropathy: its diagnosis and prognosis. *Clin Endocrinol Metab* **1986**; *15*:855–888.
14. Cohen S., Wiliamson C.M. Perceived stress in a probability sample of the United States, in S. Spacapam, S. Oskamp (eds.) The social psychology oh health: Claremont Symposium on applied social psychology, London, Sage, 1988.
15. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation***. 2009**; *120*:1640-5.
16. Di Angelantonio E, Bhupathiraju S, Wormser D, Gao P, Kaptoge S, Berrington de Gonzalez A, et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet.* **2016**; *388*(10046):776–86.
17. Heart rate variability: standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation*. **1996**; *93*(5): 1043–1065.
18. Constantinescu V.; Matei D.; Constantinescu I.; et al. Heart rate variability and vagus nerve stimulation in epilepsy patients. *Translational Neuroscience* **2019** , *10*,1 Pages: 223-232
19. Bamia C, Trichopoulou A, Lenas D, Trichopoulos D. Tobacco smoking in relation to body fat mass and distribution in a general population sample. *Int J Obes Relat Metab Disord*. **2004**; *28*(8):1091-6.

20. Canoy D, Wareham N, Luben R, Welch A, Bingham S, Day N, Khaw KT. Cigarette smoking and fat distribution in 21,828 British men and women: a population-based study. *Obes Res*. **2005**; *13*(8):1466-75.
21. J Audrain-McGovern , N L Benowitz. Cigarette smoking, nicotine, and body weight. *Clin Pharmacol Ther* **2011**; *90*(1):164-8.
22. Barutcu I, Esen AM, Kaya D, Turkmen M, Karakaya O, Melek M, et al. Cigarette smoking and heart rate variability: dynamic influence of parasympathetic and sympathetic maneuvers. *Ann Noninvasive Electrocardiol*. **2005**; *10*(3):324–9.
23. Cagirci G, Cay S, Karakurt O, Eryasar N, Kaya V, Canga A, et al. Influence of heavy cigarette smoking on heart rate variability and heart rate turbulence parameters. *Ann Noninvasive Electrocardiol*. **2009**; *14*(4):327–32.
24. Lee CL, Chang WD. The effects of cigarette smoking on aerobic and anaerobic capacity and heart rate variability among female university students. *Int J Womens Health*. **2013**; *5*: 667–79.
25. Middlekauff HR, Park J, Moheimani RS. Adverse effects of cigarette and noncigarette smoke exposure on the autonomic nervous system: Mechanisms and implications for cardiovascular risk. *J Am Coll Cardiol*. **2014**; *64*(16): 1740–50
26. J. Dratva, N. Probst-Hensch, A. Schmidt-Trucksäss et al. Atherogenesis in youth--early consequence of adolescent smoking. *Atherosclerosis*, **2013**, *230*, no. 2.
27. Straznicky NE, Nestel PJ, Esler MD. Autonomic Nervous System: Metabolic Function. *Elsevier* **2009**: p. 951-959.
28. Lago F, Dieguez C, Gomez-Reino J, Gualillo O. Adipokines as emerging mediators of immune response and inflammation. *Nature Clinical Practice Rheumatology*. **2007**; *3*:716-24.
29. Borer KT. Counterregulation of insulin by leptin as key component of autonomic regulation of body weight. *World J Diabetes* **2014**; *5*(5): 606-629.
30. Niswender K.D., Magnuson M.A. Obesity and the beta cell: lessons from leptin. *J. Clin. Invest*. **2007**; *117*: 2753–2756.
31. D. Langin. Adipose tissue lipolysis is a metabolic pathway to define pharmacological strategies against obesity and the metabolic syndrome. *Pharmacological Research*, **2006**, *53*,6, pp. 482–491.
32. J. Lee and J. P. Cooke. The role of nicotine in the pathogenesis of atherosclerosis. *Atherosclerosis*, **2011**, *215*, 2, pp. 281–283.
33. R. D. Egleton, K. C. Brown, and P. Dasgupta. Angiogenic activity of nicotinic acetylcholine receptors: implications in tobacco-related vascular diseases. *Pharmacology & Therapeutics*, **2009**, *121*, no. 2, pp. 205–223.
34. H. L. Luo, W. J. Zang, J. Lu, X. J. Yu, Y. X. Lin, and Y. X. Cao. The protective effect of captopril on nicotine-induced endothelial dysfunction in rat. *Basic & Clinical Pharmacology & Toxicology*, **2006**, *99*, no. 3, pp. 237–245.
35. M. S. Zhou, K. Chadipiralla, A. J. Mendez et al. Nicotine potentiates proatherogenic effects of oxLDL by stimulating and upregulating macrophage CD36 signaling. *American Journal of Physiology: Heart and Circulatory Physiology*, **2013**, *305*, no. 4, pp. H563–H574.
36. Harte CB, Meston CM. Effects of Smoking Cessation on Heart Rate Variability Among Long-Term Male Smokers. *Int J Behav Med*. **2014**; *21*(2):302–9.