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Unstimulated Salivary Secretion and Heart Rate Variability in Healthy Subjects

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Abstract

Background. *Unstimulated salivary flow rate (USFR) has a close relationship with the sympathetic-parasympathetic activities of the autonomic nervous system (ANS). The heart rate variability (HRV) allows knowing the balance between the sympathetic and parasympathetic activities of the ANS.*

Objective: *The objective of this work was to examine the relationship between USFR and the balance of sympathetic and parasympathetic activities of the ANS assessed by measuring HRV.*

Materials and Methods: *Fifty-six healthy subjects were studied divided into two groups according to a higher level (A) or lower (B) USFR. The USFR and the VFC were measured consecutively. The Pearson correlations of the variables of the intensity and frequency domains of the HRV with the values of the USFR of the whole group and either the groups with smaller or higher USFR were calculated. Values with p< 0.05 were considered statistically significant.*

Results: *The USFR of subjects with lower USFR correlated positively and significantly with PNN50 (p< 0.001), RMSSD (p< 0.001) and HF (p= 0.0183); and in a negative and significant way with the LF (p= 0.0182); while in the subjects of the total group and the group with higher USFR, it did not correlate significantly with the HRV parameters.*

Conclusions: *The results obtained allow us to propose that in healthy subjects with lower USFR, the sympathetic-parasympathetic activity relationship of the ANS plays a critical role in the control of USFR; while in subjects with greater USFR, other factors may have a role preponderant.*

Keywords: *non-stimulated salivary secretion, autonomic nervous system, heart rate variability.*

Introduction

The understanding of the factors involved in the regulation of salivary secretion is critical given the numerous disorders that involve dry mouth (xerostomia) and hypo salivation and their consequences on oral health, especially in chronic diseases.[1] The autonomic nervous system activity plays a fundamental role in the regulation of salivary flow rate.[2] The heart rate variability (HRV) is a physiological characteristic related to the influence of the autonomic nervous system (ANS) on the heart rate, and it is a valuable tool as a predictor and evolution factor of several disorders that involve ANS disorders.[3] HRV is evaluated by analyzing RR intervals in electrocardiographic

records. The HRV indices are calculated in the time or frequency domains through different algorithms.[4] To evaluate the sympathetic/parasympathetic balance of the SNA the use of bands in the frequency domain is recommended: high frequency (HF), low frequency (LF) and the relationship LF/HF.[5,6]

Physiological and pathophysiological variations of unstimulated salivary flow rate (USFR) could be related to the predominance of sympathetic or parasympathetic activity of ANS.[7] Therefore, it is postulated that in healthy subjects, USFR within physiological ranges could be related to the sympathetic-parasympathetic balance of the ANS. This study aimed to analyze the correlation of the USFRwith the time domain and frequency parameters of HRV in healthy subjects with different USFRbaseline rates.

Materials and Methods
Population
We studied 56 healthy subjects of the community of students of the educational institution. The inclusion criteria were no ingestion of medications in a previous period of 3 days, no smoking, and without apparent diseases. The study was conducted by following the criteria of human research of the Declaration of Helsinki,[8] and was approved by the Institutional Ethics Committee (2.2.2018-3) and all subjects gave their written informed consent.

Measurement of unstimulated salivary flow rate (USFR)
The USFRwas measured by Whatman paper strips of 1x17 cm wrapped in a low-density polyethylene bag, sterilized with ethylene oxide and millimeter from the second centimeter.[9]

Heart rate variability
The heart rate variability was assessed in the morning between 9:00 and 11:00 a.m. in a quiet study room with an ambient temperature of 25 °C, with the participant lying in the supine position. The participants received a detailed explanation of the process. After a rest period of 10 minutes, an electrocardiogram was recorded for 5 minutes. The segments of the 5-minute electrocardiogram were amplified, digitized, and stored in a computer, using the Sphygmo Cor device (At Cor Medical, Model EM3, Sydney, Australia). The device considers only normal heartbeats, ignoring ectopic beats, to derive the statistics from the parameters of the normal R-R intervals (N-N intervals) of the electrocardiogram. The power domain variables included the PNN50 which is the number of successive differences of the NN intervals that differ by more than 50 ms expressed as a percentage of the total number of ECG cycles analyzed and expressed as a percentage. Also, the RMSSD that represent the mean quadratic difference of the NN intervals. The frequency domain variables obtained from the spectral analysis of successive NN intervals that include: high-frequency power (HF) and low-frequency power (LF).[10,11]

Statistical Analysis
We examined the Pearson correlations between the time indices (PNN50 and RMMSD) and frequency (LF and HF) of HRV with the USFR, of the whole group (GT), group A with lesser salivary flow rate, and group B with higher salivary flow rate. Statistical analyses were performed using SPSS 12.0 for Windows, and statistical significance was determined at a level of p< 0.05. For the analysis, the total sample and its division into two groups were considered: A with lesser salivary flow rate and B higher salivary flow rate, using the median of USFR (1.48 ml). The data are reported as mean ± standard deviation. The analysis was performed using the Pearson correlation coefficient to observe the relationships between the USFRand the values of the time and frequency domain parameters of the HRV. The analysis was performed with SPSS 16.0 software (IBM SPSS, USA). A p-value <0.05 was considered significant.

Experimental procedure
All records were made with subjects in a supine position.
1. Rest period 10 min.
2. Unstimulated salivary flow rate record (USFR).
3. ECG record of 5 min.

Results

Population

The characteristics of the groups studied: whole group (GT), group A with lesser salivary flow rate (< 1.48 ml) and group B higher salivary flow rate (> 1.48 ml) are shown in Table I.

Table I. Demographic characteristics of the total group and groups A with lesser salivary flow rate (<1.48 ml) and B with higher salivary flow rate (> 1.48 ml)

Parameter	Whole (n=56)	Group A (n=28)	Group B (n=28)
Woman	37 (66.1%)	21 (75.0%)	16 (57.1%)
Men	19 (33.9%)	7 (25.0%)	12 (42.9%)
Age (mean ± SD)	21.6 ± 2.1	21.2 ± 1.9	21.7 ± 2.3

Heart rate variability

The time and frequency values of the heart rate variability in the groups studied are shown in Table II.

Table II. Time and frequency parameters of the heart rate variability in the three groups studied.

	Whole group	Group A	Group B	*p*
Time domain				
PNN50	35.6 ± 19.0	34.6 ± 19.8	36.5 ± 18.6	0.7105
RMSSD	56.2 ± 24.0	55.6 ± 24.9	56.9 ± 23.5	0.8407
Frequency domain				
HF	56.8 ± 20.5	51.7 ± 21.8	61.8 ± 18.0	0.0638
LF	43.2± 20.1	48.3 ± 21.9	38.2 ± 17.9	0.0431*

A= group with minor salivary flow rate.
B= group with greater salivary flow rate.
PNN50= number of adjacent intervals that vary by more than 50 ms expressed as a percentage. RSSMD = square of the middle root of the union of the adjacent R-R intervals.
HF= high frequency and LF = low frequency of the heart rate variability.
r= Pearson's correlation coefficient.
p= value of the comparison of groups A with lower salivary rateand B with higher salivary rateby the t-student test.
* p<0.05 of the comparison between groups A versus B.

The comparison between groups A (lower USFR) and B (higher USFR) showed that the LF index was significantly lower (p= 0.0431), and the HF index was higher in a constant way, but not significantly (p= 0.0638), which shows a tendency to greater parasympathetic activity in subjects of group B (higher USFR).

Pearson correlation coefficients between salivary flow rate and frequency domain parameters in the groups studied

The Pearson correlation coefficients of the studied groups: total, group A with lower lesser salivary flow rate and group B with higher salivary flow rate are shown in tables III, IV, and V; respectively.

The group of subjects studied did not show significant Pearson correlations between the USFRwith the time and frequency parameters of the HRV, see Table III.

Table III. Pearson correlations of unstimulated salivary flow rate with time domain and frequency parameters of heart rate variability in the total group of healthy subjects.

	r	*P*
Time domain		
PNN50	0.2569	0.0559
RMSSD	0.2030	0.1334
Time frequency		
HF	0.2232	0.0982
LF	-0.2237	0.0975

PNN50= number of adjacent intervals that vary by more than 50 ms expressed as a percentage, RSSMD is the square of the middle root of the union of the adjacent R-R intervals.
HF= high frequency, LF = low frequency of the HRV
r= Pearson's correlation coefficient.
p= significance value of the Pearson correlation.

The Pearson correlation analysis showed a positive and significant correlation with the PNN50 index (p <0.001), RMSSD (p <0.001), HF (p = 0.0183) in group A of subjects with lower USFR; and negative and significant with the LF index (p = 0.0182), see Table IV.

Table IV. Pearson correlations of unstimulated salivary flow rate with time domain and frequency parameters of heart rate variability in group A of healthy subjects with lesser salivation.

	r	*p*
Time domain		
PNN50	0.7009	< 0.001*
RMSSD	0.7467	< 0.001*
Frequency domain		
HF	0.4428	0.0183*
LF	-0.4431	0.0182*

PNN50= number of adjacent intervals that vary by more than 50 ms expressed as a percentage, RSSMD is the square of the middle root of the union of the adjacent R-R intervals.
HF= high frequency, LF = low frequency of the HRV
r= Pearson's correlation coefficient.
p = significance value of the Pearson correlation.
* *p*< 0.05

The Pearson correlation analysis of group B did not show significant correlations between the USFRwith the time and frequency parameters of the HRV, see Table V.

Table V. Pearson correlations of unstimulated salivary flow rate with time domain and frequency parameters of heart rate variability in group B of healthy subjects with higher salivation.

	r	p
Time domain		
PNN50	0.2648	0.1733
RMSSD	0.2159	0.2698
Frequency domain		
HF	-0.0210	0.9157
LF	0.0199	0.9199

PNN50= number of adjacent intervals that vary by more than 50 ms expressed as a percentage, RSSMD is the square of the middle root of the union of the adjacent R-R intervals.
HF= high frequency, LF = low frequency of the HRV
r= Pearson's correlation coefficient.
p= significance value of the Pearson correlation.

Discussion

According to the literature research, this is the first study in which the relationship between USFRand HRV in healthy subjects is analyzed. The results of this study are consistent with a previous report on the effect of chewing on the parasympathetic/ sympathetic balance evaluated through HRV, which found that chewing modified the sympathetic tone and stimulated salivary flow rate.[13] In another study, it was reported that the action of swallowing saliva was capable of modifying the HRV.[14] On the other hand, it has been reported that people with Sjögren's syndrome present a parasympathetic/sympathetic dysfunction, which agrees with a decrease in parasympathetic activity.[15,16]

On the other hand, the RMSSD and pNN50 time-domain indices of the HRV are directly related to the parasympathetic activity rate of the ANS.[10,17] Regarding the parameters of the frequency domain of the HRV, there is agreement that the HF index represents parasympathetic activity; while the LF index, although more complex, is commonly accepted to have a dominant sympathetic component.[11] Therefore, the set of the PNN50, RMSSD and HF indices are parasympathetic tone markers.[18]

Therefore, the findings of this research showed that subjects in the group with lesser USFRhad greater sympathetic activity as indicated by the highest values of the LF index; respect to the whole population or the group with higher USFR. On the other hand, Pearson's analysis in each of the three groups studied showed that the subjects of group A of lower USFR had time domain and frequency parameters of HRV correlated positively with the rate of parasympathetic activity. Otherwise, no significant correlations between sympathetic-parasympathetic equilibrium and USFR were observed in subjects in group B with higher USFR. It is likely that other factors regulating salivary secretion, such as non-cholinergic neuropeptides, the vasointestinal peptide, and the spinophilin regulatory protein, come into play in subjects with higher USFR.[19]

Moreover, it has been reported that the pilocarpine parasympathomimetic drug has therapeutic potential in people with Sjögren syndrome,[20] which coincides with the findings of this study in which people with low salivary flow rate have HRV values that indicate a decrease in the parasympathetic activity rate.

Conclusions

The comparative analysis of the Pearson correlations between two groups of healthy subjects with different USFRand the time and frequency parameters of the HRV showed that the USFRis directly related to the parasympathetic activity of the ANS in the subjects with lesser USFR; but not with subjects with higher USFR. Additional research should be conducted to study the influence of other USFRregulatory factors beyond the sympathetic-parasympathetic balance of ANS, especially in subjects with higher salivary flow rate.

Conflict of Interest

The authors declare that there are no competing interests. All the authors read and approved the final version.

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