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Significance of Time-Domain Measurements of Heart Rate Variability in Burning Mouth Syndrome

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Abstract: *Burning mouth syndrome (BMS) is characterized by oral burning or painful sensations without pathological changes; its real cause is unknown. We previously reported that autonomic lability was probably associated with the pathogenesis of BMS based on the results of frequency analysis of heart rate variability (HRV). HRV is composed of time and frequency domains, although the significance of the time-domain measurements of HRV in BMS has not been discussed. In this study we assessed the significance of the time-domain measurements, particularly in relation to autonomic lability. Twenty-two patients received stellate ganglion near-infrared irradiation (SGR), and the response to SGR was examined by time-domain measurements. No significant difference in the time domain was found between patients in whom SGR was effective and those in whom SGR was ineffective for BMS. We proposed several new parameters that were defined as the differences in previously established parameters between just before and after irradiation. Two of these parameters, the differential mean heart rate (D Mean HRT) and differential root mean square of successive NN interval differences (D RMSSD), reflected the relieving effects of SGR. The time-domain measurements revealed that autonomic lability, particularly parasympathetic modulation, was associated with BMS, because the parameters are considered indicative of parasympathetic responsiveness to SGR. Therefore, time-domain measurements are very useful for follow-up of BMS and for determination of the therapeutic efficacy of SGR.*

Keywords: *Time domain, Heart rate variability, Burning mouth syndrome, Autonomic lability, Stellate ganglion near-infrared irradiation*

I. Introduction

Burning mouth syndrome (BMS) is mainly characterized by oral burning or painful sensations without significant pathological changes in the oral mucosa [1-3]. The factors related to BMS are generally considered to be aging, postmenopausal climacteric disorders, oral dryness, vitamin deficiency, anemia, drugs, and psychosocial disorders [4]; a relationship between BMS and the function of the autonomic nervous system (ANS) has also been pointed out recently [5]. Heart rate variability (HRV) is a phenomenon of pulse-to-pulse variations in pulse rate and reflects ANS functions: sympathetic and parasympathetic activities [6,7]. HRV is a kind of biosignal for ANS functions; its analysis is useful to assess autonomic activity and to diagnose autonomic neuropathy [7-11]. We previously experienced a rare case of BMS induced by stress during dental therapy and monitored by HRV analysis; the HRV parameters indexing autonomic activity were well correlated with the appearance of BMS [12]. In addition, we found that the diverse autonomic responses to stellate ganglion near-infrared irradiation (SGR) between BMS patients were related to the possibility of remission of symptoms [13]. In our previous study, we proposed several new parameters: the differential normalized low-frequency (D LF norm), differential normalized high-frequency (D HF norm), and differential low-frequency/high-frequency ratio (D LF/HF). These were respectively originated from the frequency-domain parameters of HRV: normalized low-frequency (LF norm), normalized high-frequency (HF norm), and low-frequency/high-frequency ratio (LF/HF) [13], which are generally used as indices of sympathetic activity, parasympathetic activity, and autonomic balance, respectively [14-16]. Our proposed parameters were considered indices of autonomic responsiveness, since they were defined as the deference in the original parameters between just before and after stimuli such as SGR [13]. Our proposed parameters were shown to reflect the relieving effects of SGR on BMS, that is, D LF norm and D LF/HF decreased, while D HF norm increased along with the amelioration of symptoms [13]. We suggested that the nature of BMS, that is, not

autonomic imbalance but autonomic lability, played an important role in the pathogenic and healing process of BMS [13]. HRV is composed of time and frequency domains [7], and the relationship between the frequency domain and chronic pain has been widely investigated. On the other hand, the relationship between the time domain and chronic pain has rarely been discussed in the field of chronic pain, even though the time domain is the first parameter used and the simplest means of calculating HRV [7]. In this study, we investigated whether the time domain of HRV could explain the autonomic lability in BMS; for this purpose, we assessed the significance of the time-domain measurements of HRV in BMS.

II. Methods

The study was approved by an Institutional Review Board, Medical Ethics Committee of Tokushima University Hospital. All patients provided their informed consent after a full explanation of all procedures and were recruited for this study.

Patient selection

Patients attended the Department of Oral Medicine, Tokushima University Hospital, from January 2010 to December 2012 and were diagnosed as BMS according to the following criteria: 1) presence of pain or a burning sensation on the surface of the tongue; 2) absence of local or systemic disease related to the above tongue symptoms, such as candidiasis, xerostomia, glossitis, anemia, neuralgia, diabetes mellitus, and referred pain from dentalgia; 3) absence of somatization of a psychiatric disorder; and 4) absence of pain medication.

Stellate ganglion near-infrared irradiation and time-domain measurements of heart rate variability

All patients received SGR under the following conditions: power of 5.0 W, pulse irradiation, duration of 3 min, and once a week for 10 weeks. The response to SGR was examined by time-domain measurements of HRV just before and after every irradiation, and evaluated with a visual analogue scale (VAS: 0-100 mm) representing glossalgia intensity. An irradiation device (SUPER LIZER PX Type 2; Tokyo Iken Co. Ltd., Tokyo, Japan) and HRV analyzer (SA-3000P; Tokyo Iken Co. Ltd.) were used for the SGR and HRV analysis, respectively. The HRV analyzer resembles a pulse oxymeter and analyzes pulse-to-pulse variations in pulse rate by a built-in HRV analyzing system; it enables rapid and accurate measurements of autonomic activity without subjecting patients to any stress. The relieving effects of SGR were assessed for the first and second half of the total treatment period, with each half consisting of 5 treatments in 5 weeks. The 1st and 2nd VAS values were thus the mean values of VAS in each period. Complete response (CR), partial response (PR), no change (NC), or progressive disease (PD) was defined as a 100%, $\geqq$50%, <50%, or $\leqq$0% decrease in the 2nd VAS value compared to the 1st one, respectively. In addition, cases of CR and PR, and those of NC and PR, were defined as effective and ineffective, respectively.

The following time-domain HRV variables were obtained from the variation in the beat-to-beat interval [7]: the mean heart rate (Mean HRT), standard deviation of all NN intervals (SDNN), root mean square of successive NN interval differences (RMSSD), and physical stress index (PSI). Approximate entropy (ApEn) was also measured as a nonlinear index.

The following parameters were newly proposed: the differential mean heart rate (D Mean HRT), differential standard deviation of all NN intervals (D SDNN), differential root mean square of successive NN interval differences (D RMSSD), differential physical stress index (D PSI), and differential approximate entropy (D ApEn). D Mean HRT was defined as the differential between the Mean HRT values just before and after irradiation. D SDNN, D RMSSD, D PSI, and D ApEn were defined as indices of responsiveness to SGR as well as D Mean HRT.

Statistical analysis

Statistical analyses were carried using Excel-Toukei 2010 (Social Survey Research Information Co. Ltd., Tokyo, Japan) and the paired Student's t-test for intergroup comparisons or unpaired Student's t-test for within-group comparisons. A value of $P<0.05$ was considered statistically significant.

III. Results

Table 1 shows all selected patients with BMS. Patients were 22 Japanese females; their age ranged of from 45 to 82 years old, with an average of 64.8 years old. They all complained about night pain but did not suffer from distinct allodynia or hyperalgesia.

Figure 1 shows the time course of the VAS values. In 9 patients (40.9%), SGR was judged to be effective based on the differential between the 1st and 2nd VAS values, as shown in Figure 2.

Table 2 shows the scores of the time-domain HRV variables and nonlinear index during SGR. The mean value is shown for each parameter: the Mean HRT, SDNN, RMSSD, PSI, and ApEn. No significant differences in any of variables were found within the groups or between the groups.

Table 1 Clinical characteristics and results of SGR in the 22 patients of the series

Case No.	Age/ Gender	Glossalgia Duration	Glossalgia Type	Glossalgia Severity	Glossalgia Site	Complication	Results of SGR
1	63/F	51	Spont	Mild	Apex	NP	PR
2	82/F	0	Spont	Mild	Apex	AP, HT	PR
3	67/F	18	Spont	Distressing	Apex	HL, SD	PR
4	58/F	2	Spont	Mild	Apex	Asthma	PR
5	64/F	1	Spont	Mild	Whole	Asthma, HT, Insomnia, Glaucoma, NA	CR
6	56/F	3	Spont	Mild	Whole	NP	PR
7	72/F	36	Spont, Induc	Discomfort	Apex, Dorsum	CG, HL, Insomnia	PR
8	76/F	7	Spont	Discomfort	Apex, Marginal	HT	PR
9	51/F	12	Spont	Mild	Whole	NP	PR
10	65/F	46	Spont	Distressing	Apex, Dorsum, Marginal	GU	NC
11	79/F	13	Spont	Distressing	Dorsum	NP	PD
12	68/F	29	Spont, Induced	Mild	Apex	HT, Insomnia, NA	NC
13	68/F	41	Spont	Mild	Apex	HT, Insomnia, NA	NC
14	62/F	48	Spont	Distressing	Marginal	HT, Insomnia, NA	NC
15	60/F	0	Spont	Mild	Whole	HT	NC
16	63/F	0	Spont	Excruciating	Marginal	Glaucoma, Insomnia, SCS	NC
17	76/F	0	Induced	Distressing	Marginal	Constipation, HT, Insomnia	NC
18	59/F	12	Spont	Mild	Apex	HL	NC
19	63/F	19	Spont, Induced	Mild	Apex	Insomnia, RA	NC
20	55/F	6	Spont	Distressing	Apex, Dorsum	NA	PD
21	62/F	3	Spont, Induced	Discomfort	Apex	CG, HL	NC
22	49/F	9	Spont, Induced	Discomfort	Apex, Dorsum	NP	NC

AP, angina pectoris; CG, chronic gastritis; CR, complete response; GU, gastric ulcer; HL, hyperlipidemia, HT, Hypertension; NA, nasal allergy; NC, no change; NP, no particular; PD, progressive disease; PR, partial response; RA, rheumatoid arthritis; SCS, spinal canal stenosis; SD, sudden deafness; SGR, stellate ganglion near-infrared irradiation; Spont, spontaneous. Glossalgia duration was expressed in months. Glossalgia severity was excerpted from the standard long-form McGill Pain Questionnaire.

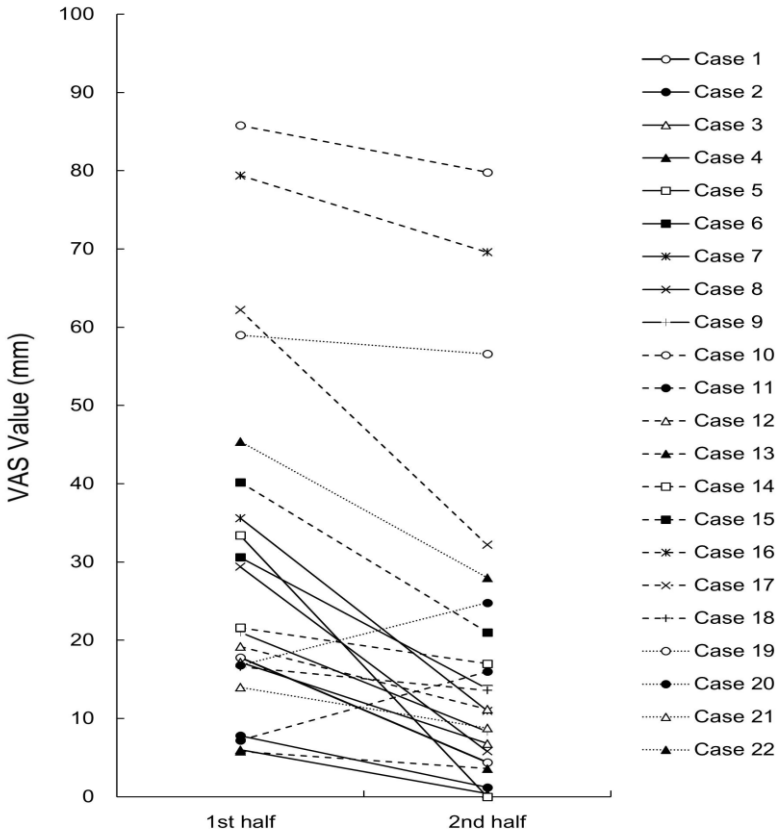

Figure 1 Time course of VAS values. VAS, visual analogue scale; 1st half, the 1st half of the treatment period; 2nd half, the 2nd half of the treatment period.

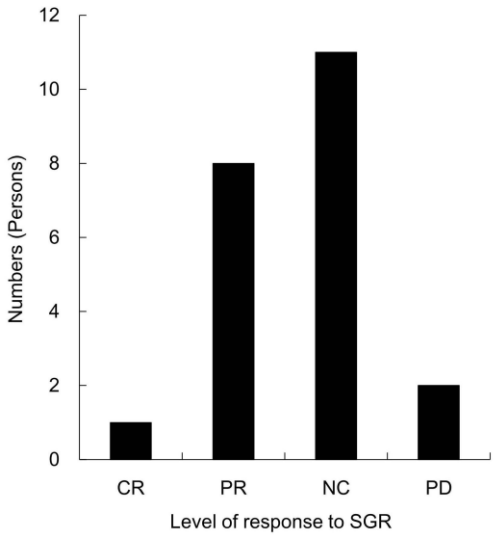

Figure 2 Results of SGR. SGR, stellate ganglion near-infrared irradiation; CR, complete response; PR, partial response; NC, no change; PD, progressive disease.

Table 2 Scores of time-domain HRV variables during SGR

	Effective group (n=9)		Ineffective group (n=13)	
	1st half[1]	2nd half[2]	1st half	2nd half
Mean HRT (bpm)[3]	68.0 ± 9.6	69.0 ± 8.2	68.3 ± 7.3	69.4 ± 6.5
SDNN (ms)[4]	33.4 ± 12.1	34.3 ± 9.5	31.8 ± 7.8	34.0 ± 12.4
RMSSD (ms)[5]	25.4 ± 11.4	23.6 ± 10.2	25.9 ± 10.7	28.3 ± 15.3
PSI[6]	89.4 ± 96.6	72.5 ± 57.4	71.0 ± 37.2	74.5 ± 43.8
ApEn[7]	1.01 ± 0.05	0.97 ± 0.06	0.98 ± 0.05	0.98 ± 0.06

Scores are the mean values of time-domain HRV variables: Mean HRT, SDNN, RMSSD, PSI and ApEn. No significant difference in each variable was found within the groups and between the groups. HRV, heart rate variability; SGR, stellate ganglion near-infrared irradiation. [1]1st half of the treatment period, [2]2nd half of the treatment period, [3]Mean heart rate, [4]Standard deviation of all NN intervals, [5]Root mean square of successive NN interval differences, [6]Physical stress index, [7]Approximate entropy.

Table 3 Scores of differential time-domain HRV variables during SGR

	Effective group (n=9)		Ineffective group (n=13)	
	1st half[1]	2nd half[2]	1st half	2nd half
D Mean HRT (bpm)[3]	-0.8 ± 1.2	-1.8 ± 1.3*	-1.7 ± 0.9	-1.6 ± 1.4
D SDNN (ms)[4]	1.37 ± 3.16	-1.03 ± 3.24	0.72 ± 3.84	0.46 ± 4.85
D RMSSD (ms)[5]	-0.39 ± 4.70	2.89 ± 3.68*	0.16 ± 3.12	-0.82 ± 4.08†
D PSI[6]	1.18 ± 23.42	-2.82 ± 32.01	-5.80 ± 13.87	-4.67 ± 11.94
D ApEn[7]	0.00 ± 0.04	0.00 ± 0.05	-0.04 ± 0.05	-0.02 ± 0.05

Scores are the mean values of differential time-domain HRV variables: D Mean HRT, D SDNN, D RMSSD, D PSI and D ApEn. *Significantly different ($P<0.05$) within the group. †Significantly different ($P<0.05$) between the groups. HRV, heart rate variability; SGR, stellate ganglion near-infrared irradiation. [1]1st half of the treatment period, [2]2nd half of the treatment period, [3]Differential mean heart rate, [4]Differential standard deviation of all NN intervals, [5]Differential root mean square of successive NN interval differences, [6]Differential physical stress index, [7]Differential approximate entropy.

Table 3 shows the scores of the differential time-domain HRV variables and nonlinear index during SGR. The mean value is shown for each parameter: the D Mean HRT, D SDNN, D RMSSD, D PSI, and D ApEn. The mean value of the 1st D Mean HRT, representing the mean value of D Mean HRT of the 1st half of the treatment period, was -0.8 ± 1.2 bpm, whereas that of the 2nd one was -1.8 ± 1.3 bpm in the effective group. The mean value of the 1st D Mean HRT was significantly higher ($p<0.05$) than that of the 2nd one. The mean value of the 1st D RMSSD, representing the mean value of D RMSSD of the 1st half of the treatment period, was -0.39 ± 4.70 ms, whereas that of the 2nd one was 2.89 ± 3.68 ms in the effective group. The mean value of the 1st D RMSSD was significantly lower ($p<0.05$) than that of the 2nd one. On the other hand, the mean value of the 2nd D RMSSD was -0.82 ± 4.08 ms in the ineffective group; the mean value of the 2nd D RMSSD in the effective group was significantly higher ($p<0.05$) than that in the ineffective group.

Figure 3 shows the time courses of D Mean HRT in the effective group. The mean value of the 1st D Mean HRT was -0.8 ± 1.2 bpm, whereas that of the 2nd one was -1.8 ± 1.3 bpm. The mean value of the 1st D Mean HRT was significantly higher ($p<0.05$) than that of the 2nd one.

Figures 4A and 4B show the time courses of D RMSSD in the effective group and the ineffective group, respectively. The mean value of the 1st D RMSSD in the effective group was -0.39 ± 4.70 ms, whereas the mean value of the 2nd one was 2.89 ± 3.68 ms. The mean value of the 1st D RMSSD was significantly lower ($p<0.05$) than that of the 2nd one. In the ineffective group, the mean value of the 1st D RMSSD was 0.16 ± 3.12 ms, whereas the mean value of the 2nd D RMSSD was -0.82 ± 4.08 ms; no significant difference in either variable was found within the group. On the other hand, the mean value of the 2nd D RMSSD in the effective group was significantly higher ($p<0.05$) than that in the ineffective group.

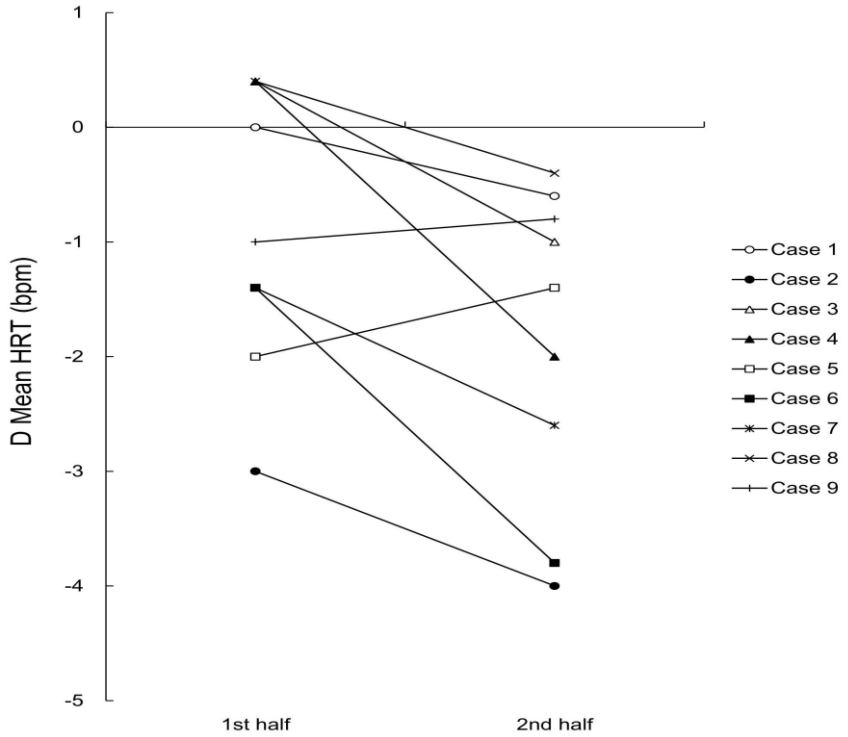

Figure 3 Time course of D Mean HRT in the effective group. D Mean HRT, differential mean heart rate; 1st half, the 1st half of the treatment period; 2nd half, the 2nd half of the treatment period.

IV. Discussion

We found that the newly proposed parameters in the time domain, notably D Mean HRT and D RMSSD, as indices of parasympathetic responsiveness to SGR revealed autonomic lability, particularly parasympathetic modulation associated with BMS.

The time domain, which is one of the components of HRV, consists of the Mean HRT, SDNN, RMSSD, PSI, ApEn, and so on; its relation to pain has been sporadically reported as described below. The heart rate, from which the Mean HRT is obtained, is determined by a complex interplay of sympathetic and HRT is extensively utilized for the index how ANS, particularly parasympathetic nerve, responds to nociceptive stimuli [19-27], and has been reported to be increased by acute pain [28]. SDNN is indicative of autonomic dysregulation and is used as an index of the ability to adjust autonomic balance [29]. Stressful conditions, e.g., acute pain, have been shown not to affect SDNN [28,30,31]. RMSSD is indexing parasympathetic activity [29,32]. Following nociceptive stimuli such as cold pressor test and acute pain, decreases in RMSSD and HF

parasympathetic activities, and is under the tonic inhibitory control of parasympathetic activity [17,18]. Mean norm are observed concurrently [32,33], and RMSSD is considered to correlate highly with HF norm [34]. These and other studies provided considerable evidence that acute pain decreases parasympathetic activity [35-37]. On the other hand, RMSSD and HF norm have not been significantly related to pain rating in sporadic reports [32,38]. PSI reflects load and pressure on the heart and is based on SDNN and Mean HRT. When Mean HRT increases and SDNN decreases under stimuli, PSI is recognized to increase. ApEn has recently been introduced to estimate the complexity of HRV and irregularity within a series of pulses [39-41]; lower values of ApEn indicate a regular signal [39,42]. The measurements of ApEn enable detection of stress conditions [43]. In this study, neither time domain: Mean HRT, SDNN, RMSSD, PSI, or ApEn, was significantly related to relieving effects of SGR, as shown in Table 2. On the other hand, a significant difference in the time domain concerning D RMSSD was found between SGR effective and ineffective BMS, as shown in Table 3. Furthermore, significant change of the time domain concerning D Mean HRT and D RMSSD was found during irradiation in SGR effective BMS, as shown in Table 3. Given that D Mean HRT and D RMSSD are related to parasympathetic activity, and that they are defined as the deferential of the original parameters between just before and after stimuli such as SGR, we suggest that autonomic lability, particularly its parasympathetic component, plays an important role in the pathogenic and healing process of BMS. Our findings correspond to a previous report in which BMS patients were found to have decreased parasympathetic activity rather than increased sympathetic activity [44]. Meanwhile, in our previous study, D LF norm, D HF norm, and D LF/HF were shown to reflect relieving effects of SGR on BMS [13]. The change in the parameters suggests a correction of abnormally increased sympathetic or decreased parasympathetic activity.

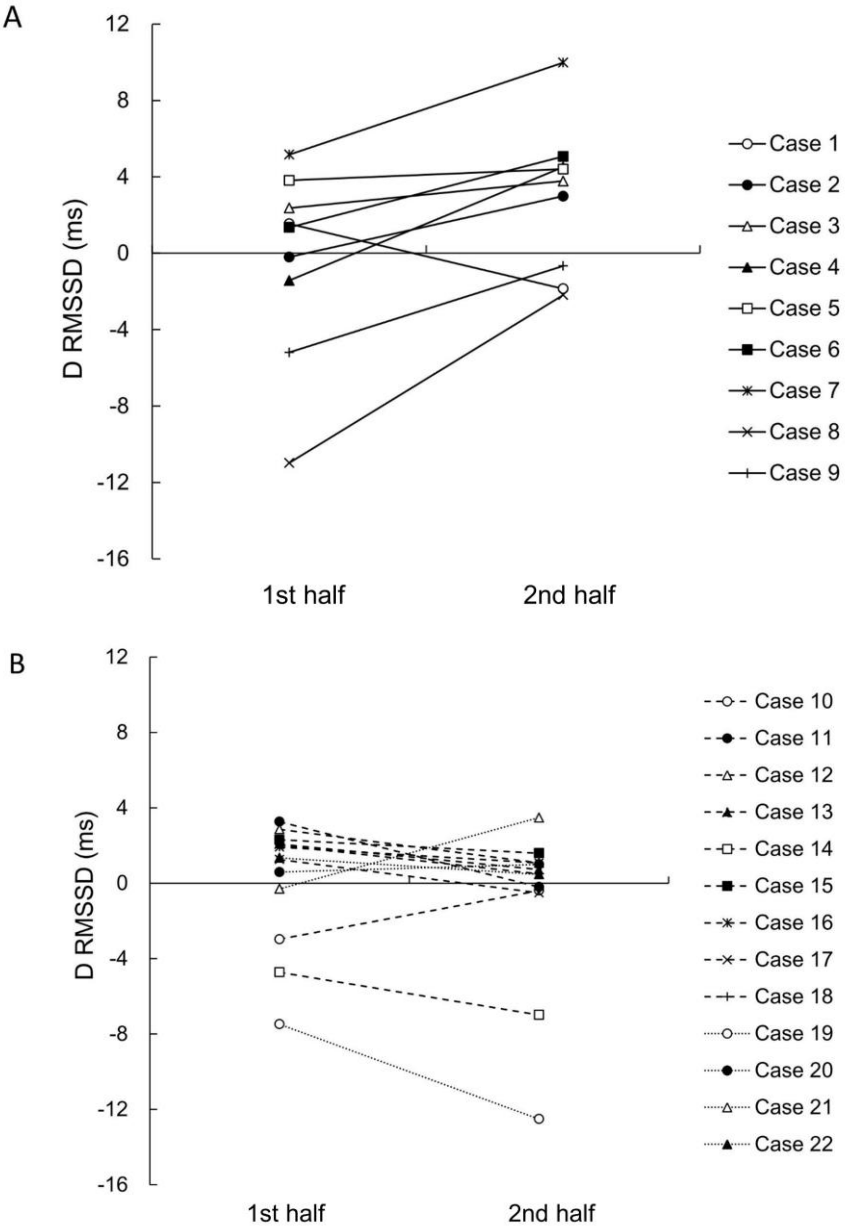

Figure 4 Time course of D RMSSD. A: effective group, B: ineffective group. D RMSSD, differential root mean square of successive NN interval differences; 1st half, the 1st half of the treatment period; 2nd half, the 2nd half of the treatment period.

SGR is considered to reduce abnormally increased sympathetic activity associated with BMS as well as stellate ganglion block (SGB) [5]. Given the functional mechanism of SGR described above, the change in the parameters may suggest that SGR ameliorate the sympathetic abnormalities in BMS patients. However, this theory conflicts with the results of this study: that is, we found that autonomic lability, particularly its parasympathetic component, plays an important role in the pathogenic and healing process of BMS. However, the conflicts between the studies could be resolved, if either comparative parasympathetic activation or secondary parasympathetic change after SGR were verified. Therefore, further investigations will be needed to clarify the functional mechanism of SGR and the relationship between autonomic lability and the healing process of BMS. We experienced two types of BMS, that is, SGR effective and ineffective BMS; the difference in the efficacy between the two types was considered to be related to the theory that autonomic lability plays an important role in the pathogenic and healing process of BMS [13]. This is because the difference between the two types of BMS could be explained by using our proposed parameters, which are indices of autonomic responsiveness. In the case of SGR ineffective BMS, the failure of SGR to exert an effect on BMS, or to change the parameters, was thought to possibly involve low reactivity to SGR, unirradiated stellate ganglion, non-autonomic BMS, and so on. One of the strategies for improving low reactivity to SGR is to review the

irradiation conditions, including the irradiation power, duration, and frequency; this strategy may help to enhance the reactivity to SGR. Another strategy is to select SGB instead of SGR. The potency of SGR on ANS is thought to be lower than that of SGB because SGR incompletely blocks stellate ganglions. In fact, no patient who received SGR had distinct signs or symptoms suggestive of Horner's syndrome during irradiation. The current method of SGR is to start with detection of the 7th cervical transverse process on palpation, followed by irradiation around this area. Therefore, it is reluctantly acceptable to regard the current SGR as blind irradiation. One of the solutions to the problem of unirradiated stellate ganglions may be to develop a navigation system to assist in accurate irradiation; such a navigation system could ensure irradiation to the stellate ganglion. In the case of non-autonomic BMS, the solution could be to develop a new diagnostic procedure to identify the real causes of BMS apart from autonomic disorder, and to select an appropriate treatment for this pathological condition.

In conclusion, we found that our newly proposed parameters in the time domain, notably D Mean HRT and D RMSSD, were related to relieving effects of SGR. Based on these findings, we suggested that autonomic lability, particularly parasympathetic modulation associated with BMS, plays an important role in the pathogenic and healing process of BMS, because the parameters are considered indicative of parasympathetic responsiveness to SGR. Therefore, time-domain measurements of HRV in BMS are very useful in follow-up of BMS and for determination of the therapeutic efficacy of SGR.

V. Conclusions

The newly proposed parameters in the time domain, notably D Mean HRT and D RMSSD, were related to the relieving effects of SGR. Autonomic lability, particularly parasympathetic modulation associated with BMS, may play an important role in the pathogenic and healing process of BMS, because the parameters are considered indicative of parasympathetic responsiveness to SGR. Therefore, time-domain measurements of HRV in BMS are very useful in follow-up of BMS and for determination of the therapeutic efficacy of SGR.

Competing interests

The authors declare that they have no competing interests.

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References

[1] Cekić-Arambasin A, Vidas I, Stipetić-Mravak M (1990) Clinical oral test for the assessment of oral symptoms of glossodynia and glossopyrosis. J Oral Rehabil 17: 495-502.
[2] Femiano F, Lanza A, Buonaiuto C, Gombos F, Nunziata M, et al (2008) Burning mouth syndrome and burning mouth in hypothyroidism: proposal for a diagnostic and therapeutic protocol. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 105: e22-e27.
[3] Huang W, Rothe MJ, Grant-Kels JM (1996) The burning mouth syndrome. J Am Acad Dermatol 34: 91-98.
[4] Tourne LP, Fricton JR (1992) Burning mouth syndrome. Critical review and proposed clinical management. Oral Surg Oral Med Oral Pathol 74: 158-167.
[5] Nakase M, Okumura K, Tamura T, Kamei T, Kada K, et al (2004) Effects of near-infrared irradiation to stellate ganglion in glossodynia. Oral Dis 10: 217-220.
[6] Akselrod S, Gordon D, Ubel FA, Shannon DC, Berger AC, et al (1981) Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control. Science 213: 220-222.
[7] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation 93: 1043-1065.
[8] Johansen TL, Kambskar G, Mehlsen J (1997) Heart rate variability in evaluation of the autonomic nervous system. Ugeskr Laeger 159: 6666-6671.
[9] Lindh V, Wiklund U, Sandman PO, Hakansson S (1997) Assessment of acute pain in preterm infants by evaluation of facial expression and frequency domain analysis of heart rate variability. Early Human Development 48: 131-142.
[10] Omerbegovic M (2009) Analysis of heart rate variability and clinical implications. Med Arh 63: 102-105.
[11] Sztajzel J (2004) Heart rate variability: a noninvasive electrocardiographic method to measure the autonomic nervous system. SWISS MED WKLY 134: 514-522.
[12] Momota Y, Tomioka S, Furukita M, Satsuma T, Takano H, et al (2013) Adrenergic urticaria and glossalgia induced by stress During dental therapy and monitored by heart rate variability analysis: a case report. J Oral Maxillofac Surg Med Pathol 25: 264-266.
[13] Momota Y, Takano H, Kani K, Matsumoto F, Motegi K, Aota K, et al (2013) Frequency analysis of heart rate variability: a useful assessment tool of linearly polarized near-infrared irradiation to stellate ganglion area for burning mouth syndrome. Pain Med 14: 351-357.
[14] Doğru MT, Başar MM, Yuvanç E, Simşek V, Sahin O (2010) The relationship between serum sex steroid levels and heart rate variability parameters in males and the effect of age. Turk Kardiyol Derns Ars 38: 459-465.
[15] Malliani A, Pagani M, Lombardi F, Cerutti S (1991) Cardiovascular neural regulation explored in the frequency domain. Circulation 84: 428-492.
[16] Malliani A, Lombardi F, Pagani M (1994) Power spectrum analysis of heart rate variability: a tool to explore neural regulatory mechanisms. Br Heart J 71: 1-2.
[17] Jose AD, Collison D (1970) The normal range and determinants of the intrinsic heart rate in man. Cardiovasc Res 4: 160-167.

[18] Kannel WB, Kannel C, Paffenbarger RS, Cuppls LA Jr (1987) Heart rate and cardiovascular mortality: The Framingham Study. Am Heart J 113: 1489-1494.
[19] Benarroch EE (2001) Pain-autonomic interactions: A selective review. Clin Auton Res 11: 343-349.
[20] Benarroch EE (2006) Pain-autonomic interactions. Neurol Sci 27: 130-133.
[21] Bruehl S, Chung OY (2004) Interactions between the cardiovascular and pain regulatory systems: An updated review of mechanisms and possible alterations in chronic pain. Neurosci Biobehav Rev 28: 395-414.
[22] Colloca L, Benedetti F, Pollo A (2006) Repeatability of autonomic responses to pain anticipation and pain stimulation. Eur J Pain 10: 659-665.
[23] Loggia ML, Juneau M, Bushnell MC (2011) Autonomic responses to heat pain: Heart rate, skin conductance, and their relation to verbal ratings and stimulus intensity. Pain 152: 592-598.
[24] Möltner A, Holzl R, Strian F (1990) Heart rate changes as an autonomic component of the pain response. Pain 43: 81-89.
[25] Randich A, Maixner W (1984) Interactions between cardiovascular and pain regulatory systems. Neurosci Biobehav Rev 8: 343-367.
[26] Tousignant-Laflamme Y, Rainville P, Marchand S (2005) Establishing a link between heart rate and pain in healthy subjects: A gender effect. J Pain 6: 341-347.
[27] Zamir N, Maixner W (1986) The relationship between cardiovascular and pain regulatory systems. Ann N Y Acad Sci 467: 371-384.
[28] Terkelsen AJ, Mølgaard H, Hansen J, Andersen OK, Jensen TS (2005) Acute pain increases heart rate: Differential mechanisms during rest and mental stress. Auton Neurosci 121: 101-109.
[29] Wang Y, Zhao X, O'Neil A, Turner A, Liu X, et al (2013) Altered cardiac autonomic nervous function in depression. BMC Psychiatry 13: 187.
[30] Olsson EM, von Schéele B (2011) Relaxing on a bed of nails: An exploratory study of the effects on the autonomic, cardiovascular, and respiratory systems, and saliva cortisol. J Altern Complement Med 17: 5-12.
[31] Terkelsen AJ, Andersen OK, Mølgaard H, Hansen J, Jensen TS (2004) Mental stress inhibits pain perception and heart rate variability but not a nociceptive withdrawal reflex. Acta Physiol Scand 180: 405-414.
[32] Bendixen KH, Terkelsen AJ, Baad-Hansen L, Cairns BE, Svensson P (2012) Experimental stressors alter hypertonic saline-evoked masseter muscle pain and autonomic response. J Orofac Pain 26: 191-205.
[33] Pollatos O, Füstös J, Critchley HD (2012) On the generalised embodiment of pain: How interoceptive sensitivity modulates cutaneous pain perception. Pain 153: 1680-1686.
[34] Thayer JF, Åhs F, Fredrikson M, Sollers JJ III, Wager TD (2012) A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. Neurosci Biobehav Rev 36: 747-756.
[35] Casadei B, Cochrane S, Johnston J, Conway J, Sleight P (1995) Pitfalls in the interpretation of spectral analysis of the heart rate variability during exercise in humans. Acta Physiol Scand 153: 125-131.
[36] Goldstein DS, Bentho O, Park MY, Sharabi Y (2011) Low-frequency power of heart rate variability is not a measure of cardiac sympathetic tone but may be a measure of modulation of cardiac autonomic outflows by baroreflexes. Exp Physiol 96: 1255-1261.
[37] Moak JP, Goldstein DS, Eldadah BA, Saleem A, Holmes C, et al (2009) Supine low-frequency power of heart rate variability reflects baroreflex function, not cardiac sympathetic innervation. Cleve Clin J Med 76: S51-S59.
[38] Martin SL, Kerr KL, Bartley EJ, Kuhn BL, Palit S, et al (2012) Respiration-induced hypoalgesia: Exploration of potential mechanisms. J Pain 13: 755-763.
[39] Pincus SM (1991) Approximate entropy as a measure of system complexity. Proc Nat Acad Sci USA 88: 2297-2301.
[40] RenuMadhavi CH, Ananth AG (2010) Quantification of heart rate variability data using symbolic entropy to distinguish between healthy and disease subjects. Int J Comput Appl 8: 10-13.
[41] Richman JS, Moorman JR (2000) Physiological time-series analysis using approximate entropy and sample entropy. Am J Physiol 278: H2039-H2049.
[42] Zhou P, Sui F, Zhang A, Wang F, Li G (2010) ApEn after music therapy is lower than that before music therapy. 3rd BMEI.
[43] Melillo P, Bracale M, Pecchia L (2011) Case study: students under stress due to university examination. BioMedical Engineering OnLine 10: 96.
[44] Hanada K (2003) Glossodynia and the function of the autonomic nervous system frequency spectrum analysis of RR intervals recorded electrocardiographically. Kokubyo Gakkai Zasshi 70: 124-130.