Relationship between Malocclusion and Heart Rate Variability Indices in Young Adults
A Pilot Study

D. Ekuni; N. Takeuchi; M. Furuta; T. Tomofuji; M. Morita
Department of Preventive Dentistry, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Keywords
Malocclusion, heart rate variability, oral health-related quality of life, young adult, high frequency

Summary
Objectives: Heart rate variability (HRV) has been used to assess sympathetic and parasympathetic modulation of heart rate. Chronic stress relates to reduced HRV. Malocclusion has effects on quality of life, which can lead to chronic stress. Therefore, we hypothesized that malocclusion, as chronic stress, may contribute to reduced HRV. The aim of this study was to investigate the relationship between malocclusion and HRV indices in healthy young adults.

Methods: Thirty-seven non-smoking healthy subjects, aged 22 to 25 years, were examined. Malocclusion was defined by Angle classification. HRV indices included root mean square of successive differences, low frequency (LF), high frequency (HF) and ratio of LF to HF. The effects of malocclusion on quality of life and mental health were assessed using self-reported questionnaires, the condition-specific Oral Impacts on Daily Performances index (CS-OIDP) and the Hopkins Symptoms Checklist (HSCL), respectively.

Results: Significantly lower score of HF and higher heart rate (HR) level and CS-OIDP score were observed in subjects with malocclusion (n = 17) compared to those in the control subjects (n = 20) (P < 0.05). There was a positive correlation between HR and score of “anxiety” in HSCL (P < 0.05).

Conclusions: The data showed an association between malocclusion and lower HRV. Based on our results, orthodontic treatment might contribute not only to improvement of oral health and functional problems but also to improvement of stress and HRV indices.

Correspondence to:
Daisuke Ekuni
Department of Preventive Dentistry
Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences
2-5-1 Shikata-cho, Kita-ku
Okayama 700-8558
Japan
E-mail: dekuni7@md.okayama-u.ac.jp

1. Introduction
Heart rate variability (HRV) can be used to investigate autonomic nervous system (ANS) function [1]. Measurement of HRV provides information on the systems that influence heart rate, especially the sympathetic and parasympathetic (vagal) divisions of the ANS. Measurement of HRV includes time domain and frequency domain methods. In the time domain method, the most commonly used measures derived from interval differences include the standard deviation of the mean R-R interval (SDRR) [2] and root mean square of successive differences (RMSSD) [3]. RMSSD is a commonly used index in clinical cardiology and in psychophysiology, and is the most robust representation of vagal tone [1, 3]. Low frequency band power (LF, 0.04–0.15 Hz), high frequency band power (HF, 0.15–0.4 Hz) and its ratio are commonly measured in the frequency domain methods. The vagal activity is the major contributor of the HF component [1]. The LF component may represent either sympathetic modulation or combination of sympathetic and vagal influences [1]. The instantaneous balance between sympathetic and parasympathetic activities can be captured by the ratio between LF and HF [1]. The ratio of LF to HF is referred to a measure of “sympathovagal balance” [1]. However, the view of the ratio of LF to HF is actually controversial, as the LF domain is a combination of sympathetic and parasympathetic ANS activity components [4]. Reduced HRV has been related to a number of diseases, including ischemic heart disease [5], heart failure [6], hypertension [7], diabetes [8] and depression [9]. Research on HRV has generally focused on acute and laboratory stressors. Assessment of the impact of acute stress on HRV has been done utilizing cognitive (e.g., mental arithmetic), psychomotor (e.g., mirror tracing), physical (e.g., cold pressor) and social challenges [10, 11]. Studies on healthy individuals show that acute stress increases HR and decreases SDRR transiently [12, 13], or increases the ratio of LF to HF and decreases HF [14]. Other studies have investigated the influence of chronic psychosocial stress on HRV indices such as in insomnia [15] and posttraumatic stress disorder symptoms [16]. Continuous changes in sympathetic and parasympathetic neural impulses as chronic stress exhibit alterations in HR and cause oscillation of the R-R interval around
its mean value. There have been two major approaches how chronic psychosocial stress can be conceptualized in research on HRV [11]. One is based on the measurement of major life events and assuming experience of major events. The other approach focuses on measures of minor incidents and hassles, which suggests that minor events are more common than major events and may be more salient for the individual [17, 18]. For example, chronically stressed individuals show decreased HR and changed the ratio of LF to HF [19, 20].

Malocclusion has physical, psychological and social effects on quality of life, which can lead to chronic stress [21]. Some studies support that malocclusion may contribute to chronic stress [21–24]. Although chronic stress influences HRV indices as described above, there is little information on how malocclusion as chronic stress affects HRV indices. Therefore, we hypothesized that malocclusion leads to chronic stress and chronic stress induces reduced HRV. The aim of this pilot study was to investigate HRV indices in healthy young students with and without malocclusion. We used the condition-specific form of the Oral Impacts on Daily Performances index (CS-OIDP) to confirm chronic stress because CS-OIDP is the only oral health-related quality of life (OHRQoL) measure designed to link specific oral conditions, such as malocclusion, and impacts on quality of life [25–27]. The effects of malocclusion on mental health were also assessed using the Hopkins Symptoms Checklist (HSCL), which has been found to be a psychometrically valid and reliable indicator of anxiety and depression [28], because subjects with depression exhibit reduced HRV [9].

2. Materials and Methods

2.1 Study Sample

We enrolled 37 young adults (17 male and 20 female students at Okayama University; aged 22 to 25 years) who were interviewed by a dentist and identified as healthy subjects. The study was conducted from April, 2009 to February, 2010. The exclusion criteria were as follows: previous or current smoking, pregnancy, systemic diseases, or consumption of any drugs within the previous year. The study was approved by the Ethics Committee of Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences. After obtaining written informed consent, subjects completed written questionnaires regarding personal health, CS-OIDP and HSCL.

2.2 Questionnaires

The OIDP index assessed serious oral impacts on eight daily activities: eating, speaking, cleaning the mouth, relaxing, smiling, studying, emotion and social contact. If a subject reported an impact on any of the eight activities, the frequency of the impact (scale from 1 to 3) and the severity of its effect on daily life (scale from 1 to 3) were scored. If no impact was reported, then a zero score was assigned. Thereafter, subjects with positive impacts were asked to choose from a list of oral problems that, in their opinion, impacted their daily lives. Three problems (‘bad position of teeth’, ‘space between teeth’, and ‘deformity of mouth or face’) were considered in the analysis as CS-OIDP attributed to malocclusion [21, 24, 26]. The subjects with one or more positive answers were assigned to those having malocclusion-related impacts. The percentage of subjects with CS-OIDP score higher than zero was calculated.

The HSCL has been found to be a psychometrically valid and reliable indicator of anxiety and depression [28], and is also a well-validated self-report instrument in Japanese subjects [29]. Fifty-four questions, which measured the frequency and intensity of symptoms during the past week, were scored on a scale from 1 (not bothered) to 4 (extremely bothered). Scale scores were determined for each of the five primary symptom dimensions (somatization, obsessive-compulsive, interpersonal sensitivity, anxiety and depression) [30].

2.3 Definition of Malocclusion

This study permitted estimation of the prevalence of malocclusion using the Angle classification. The Angle classification of malocclusion is based on the anteroposterior relationship of the maxillary to the mandibular first molars [31, 32]. Because the number of subjects was small, the definition of malocclusion consisted of a two-grade scale (0 = normal occlusion; 1 = class I, class II division 1, class II division 2 or class III malocclusion). We defined severe malocclusion as Angle class II malocclusion with overjet > 6 mm and lip protrusion, or class III with negative overjet > 4 mm [24]. A dentist, who was preliminary calibrated by an orthodontist, performed the screening. The intra- and inter-Kappa values were more than 0.80, respectively, which indicates good agreement of diagnosis between examiners.

2.4 HRV Indices

For measuring HRV indices, subjects were instructed not to perform high-intensity physical effort both on the day of the test and the day before the test. All assessments took place between 3:00 p.m. and 4:00 p.m. on the same day of the week (Monday). Subjects were instructed to breathe at about 12 breaths/min using a timer, which was confirmed by visual inspection, to avoid the effect of respiratory rate component on HRV assessment [33]. It has been reported that HRV is reproducible in patients with chronic obstructive pulmonary disease only when the respiratory rate is controlled at 12 breaths/min [33] and is also stable at this rate in the healthy subjects [34]. Measurements were taken in the relaxed sitting position, which allowed an inclination to 90° in relation to the floor, and took place in a quiet room. The acquisition of HRV was done by a pulse frequency meter (Pulse Analyzer Plus, YKC Corporation, Tokyo, Japan) for five minutes. The power spectrum of R-R intervals was obtained by means of fast Fourier transformation and a sampling frequency of 1 kHz (Tas9, YKC Corporation, Tokyo, Japan). RMSSD was calculated as representing the average amplitude. The area under the spectral peaks within the ranges 0.033–0.04, 0.04–0.15, 0.15–0.4, and 0.333–0.4 Hz are defined as the very low frequency (VLF), LF, HF, and total power

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(TP), respectively. The normalized LF (n.u.) and HF (n.u.) powers were calculated by $100 \times \text{LF}/(\text{TP-VLF})$ and $100 \times \text{HF}/(\text{TP-VLF})$, respectively, as per task force recommendation [1]. The ratio of LF to HF, considered as an index of sympathetic-vagal balance, was also calculated.

### 2.5 Evaluation of BMI

BMI was computed as weight in kilograms divided by square height in meters, as HRV decreases with augmented body mass index (BMI) [35].

### 2.6 Statistical Analysis

The Student’s t test or Fisher’s exact test was used to compare parameters between subjects with malocclusion and those without. The statistical significance of associations among variables was determined by using the Pearson correlation coefficient. A $P$ value $< 0.05$ was considered significant. All data were analyzed using statistical packages (SPSS 15.0 J for Windows, SPSS Japan, Tokyo, Japan).

### 3. Results

Table 1 shows the distribution of age, gender and BMI in the study subjects. There were no significant differences in these indices between subjects with malocclusion and those without.

In all, 20 (54%) subjects had normal occlusion, 3 (8%) had class I malocclusion, 9 (24%) had class II division 1 malocclusion, none had class II division 2 malocclusion, and 5 (14%) had class III malocclusion. There were two subjects with severe malocclusion.

Table 2 shows the differences of clinical parameters between subjects with normal occlusion and those with malocclusion. HR and prevalence of impacts (CS-OIDP score $> 0$) in subjects with malocclusion were significantly higher than those in subjects with normal occlusion ($P < 0.05$). Level of HF in subjects with malocclusion was significantly lower than in subjects with normal occlusion ($P < 0.05$). There were no significant differences in the number of teeth present, RMSSD, LF, ratio of LF to HF, or HSCL scores between the two groups.

There was a positive correlation between HR and score of “anxiety” in HSCL ($P < 0.05$) (Table 3).

### 4. Discussion

HRV has been used to assess sympathetic and parasympathetic modulation of heart rate. Chronic stress relates to reduced HRV. Although malocclusion is believed to induce chronic stress, there is little information about relationship between malocclusion as chronic stress and the HRV indices. Thus, we focused on the effects of malocclusion on the HRV indices. This is the first study to assess the relationship between the HRV indices and malocclusion. HR in subjects with malocclusion was significantly higher than in subjects with normal occlusion, whereas the level of HF in subjects with malocclusion was significantly lower. HR positively correlated with score of “anxiety” in HSCL. These findings suggest that malocclusion as chronic stress may affect HRV indices.

Some studies have investigated the influence of chronic stress on HRV. The reduced HF level (n.u.) is related with chronic stress [20], which supports our study. Chronic stress is associated to in-
creased arterial pressure and to impaired autonomic regulation of cardiovascular functions [20]. To understand the possible link, a two-closed-loop model of the baroreflex system is proposed [36]. One loop involves HR and blood pressure control systems, and the other vascular tone and blood pressure control systems. The blood pressure control system is a common link to both loops. For example, anxiety disorders involve dysfunctional reactions, which are related to the hypothesized domain of baroreflex modulation [36]. In this study, relationship between malocclusion as chronic stress and HRV indices might be involved in the model of baroreflex system. Another possibility might be that brain areas involved in the regulation of HF may overlap with areas involved in stress attributed to malocclusion. A consistent pattern of brain areas is involved in the regulation of HF including limbic/striatal, central and peripheral physiological oscillators [40]. These areas overlap with areas involved in stress and anxiety forming a possible link between anxiety and heart disease. On the other hand, the importance of the emotional division of the anterior cingulate cortex, the prefrontal cortex and the striatum in cardiovagal activity is underscored by Ahs et al. [39]. However, the mechanism of relationship between HF and malocclusion may be complex and further studies are required.

Chronic stress decreases HR [19, 20]. The ratio of LF to HF decreases in subjects who perform job tasks at night (n = 22, 39 years old) [19] and increases in patients with symptoms of chronic psychological stress (n = 126, 44 years old) [20]. The ratio is not related to chronic hassles frequency (n = 50, 33 years old) [11]. In this study, HR in subjects with malocclusion increased and the ratio of LF to HF did not change. These discrepancies in study findings may be due to differences in the age of the subjects, sample size or types of chronic stress. Otherwise, the discrepancies might be attributable to shortcomings of linear methods. For example, HRV is the result of complex nonlinear interactions of different central and peripheral physiological oscillators [40].

The prevalence of impacts (CS-OIDP score > 0) in subjects with malocclusion was significantly higher than in subjects with normal occlusion. Other studies have shown the relationship between malocclusion by Angle classification and CS-OIDP score [32], which support our study. Based on these findings, it is suggested that the impact on quality of life attributed to malocclusion as chronic stress may affect ANS function.

Malocclusion is one of the most common oral disorders, and its prevalence is high in most countries [41, 42]. Moreover, malocclusion traits remain remarkably stable if patients do not receive orthodontic treatment [43]. Even though it is generally accepted that individuals seek orthodontic care because of the negative effects of malocclusion, evidence on the physical, psychological, and social consequences of malocclusion and orthodontic treatment is still controversial [44]. Our results may provide new insight into the consequences of malocclusion.

This study suggests that there is a potential use of HRV as a quantitative measure of ANS functioning in malocclusion. Based on our results, orthodontic treatment might contribute not only to improvement of oral esthetic and functional problems but also to improvement of stress and HRV indices. Furthermore, monitoring HRV indices might have advantages in investigating relationship between the other oral diseases and ANS function, and in controlling incidents and accidents during dental treatment.

We investigated whether subjects with severe depression were included in this study by using HSCL, as HRV can be influenced by depression [45]. There was no significant difference between the two groups in HSCL score and there were no severe depression cases. Therefore, we believe that depression had no influence on HRV in this study.

Our study has some limitations. First, all subjects were recruited from among the students at Okayama University, and the number of subjects was small. This may limit the ability to extrapolate these findings to the general population. Second, this study was cross-sectional. It is therefore still uncertain as to whether malocclusion is the cause of reduced HRV. Intervention studies will be needed to examine the causal relationship between malocclusion and HRV and to compare quality of life and HRV of people suffering from malocclusion before and after orthodontic treatment. Since young subjects have fewer systemic diseases and take less medication, we believe that investigating young adults may have some

| Table 3 Correlations between the HRV indices and scores of Hopkins Symptoms Checklist in all subjects (n = 37) |
|-----------------------------------------------|------------------|------------------|------------------|------------------|------------------|
| Hopkins Symptoms Checklist                  | Root mean square successive difference (ms) | Heart rate | Low frequency (LF) (n.u.) | High frequency (HF) (n.u.) | Ratio of LF to HF |
|                                             | r*       | P value | r       | P value | r       | P value | r       | P value |
| Score of “somatization”                     | -0.087   | 0.607   | -0.041  | 0.809   | -0.135  | 0.425   | 0.319   | 0.054   | -0.168  | 0.320   |
| Score of “obsessive-compulsive”             | 0.095    | 0.575   | 0.27    | 0.106   | 0.083   | 0.624   | -0.141  | 0.404   | 0.083   | 0.627   |
| Score of “interpersonal sensitivity”        | 0.305    | 0.065   | 0.068   | 0.689   | 0.074   | 0.665   | -0.081  | 0.364   | -0.022  | 0.896   |
| Score of “anxiety”                          | -0.201   | 0.233   | 0.421   | 0.009   | 0.179   | 0.289   | -0.150  | 0.375   | 0.190   | 0.256   |
| Score of “depression”                        | 0.037    | 0.827   | 0.240   | 0.153   | -0.059  | 0.728   | 0.030   | 0.861   | -0.085  | 0.616   |

* Pearson correlation coefficient

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advantage over a future cohort study. Third, the role of other factors (e.g., diet, exercise, genetic factors) that have been shown to affect HRV indices were not considered in our study. However, a previous study showed that physical activity had no association with HRV [46]. Forth, we did not investigate the stage of menstrual cycle for the female participants. Several studies have noted changes in HRV across menstrual cycle stage [47, 48]. However, this might not be a significant issue because there was no significant difference in the proportion of female between subjects with malocclusion and those without. Finally, we used only two types of questionnaires to evaluate stress. The potential associations might have benefited from additional assessment tools such as the State-Trait Anxiety Inventory and another physiological measure such as cortisol. In future study, these components should be considered.

5. Conclusion
In conclusion, subjects with malocclusion had increased CS-OIDP score and reduced HF. These results suggest that malocclusion as chronic stress might relate to HRV indices. Orthodontic treatment might contribute not only to improvement of oral aesthetic and functional problems but also to improvement of stress and HRV indices.

References