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Effect of high-frequency jet ventilation on heart rate variability

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Abstract: We investigated the effects of high-frequency jet ventilation (HFJV) on heart rate variability in nine patients during fentanyl ($10\,\mu g \cdot kg^{-1}$) anesthesia using power spectral density analysis. ECG and arterial pressure were recorded during intermittent positive pressure ventilation (IPPV) (tidal volume $8\,ml \cdot kg^{-1}$, respiratory rate 0.25 Hz) and during HFJV [5 Hz, $2.5\,kg \cdot (cm^2)^{-1}$]. The R-R interval time series obtained were analyzed by the autoregressive method, and low-frequency (LF) (0.05–0.15 Hz) power and high-frequency (HF) (0.20–0.50 Hz) power from R-R interval spectra were used for statistical comparison. LF power did not change during IPPV and HFJV ($108.8 \pm 41.6\,ms^2$ *vs* $105.8 \pm 22.4\,ms^2$, mean ± SE). HF power was detected during IPPV ($65.1 \pm 14.3\,ms^2$); however, it was not detected during HFJV. Plasma levels of norepinephrine and epinephrine were significantly higher during HFJV than during IPPV. The mean R-R interval, arterial pressure, and arterial blood gas data did not differ between IPPV and HFJV. These data indicate that, during fentanyl anesthesia, HFJV influences mainly the respiratory frequency fluctuation of heart rate variability, and they suggest that alteration of breathing patterns caused by HFJV might be involved, as well as elevated sympathetic neural outflow to the heart.

Key words: High-frequency jet ventilation, Heart rate variability, Fentanyl, Vagal nerve

Introduction

High-frequency jet ventilation (HFJV) is mechanical ventilation with stroke volumes smaller than the anatomical respiratory dead space, applied at frequencies between 1 and 10 Hz. HFJV is used for clinical anesthesia and for treating respiratory failure because of its better hemodynamic and respiratory effects as compared with conventional mechanical ventilation [1–3]. Animal studies have shown that HFJV continuously stimulates vagal afferent activity [4] and consequently inhibits phrenic nerve activity [5,6]. However, few studies have investigated this effect in humans.

Recently, frequency domain analysis of heart rate variability has been applied to evaluating autonomic neural function in the heart. Numerous experimental and clinical studies have shown that the high-frequency (HF) component (a frequency near that of the respiratory cycle) reflects vagal efferent activity (known as respiratory sinus arrhythmia) and the low-frequency (LF) component (around 0.1 Hz) reflects both sympathetic and vagal contributions [7]. In the present study, we used power spectrum density analysis to investigate the effect of HFJV on heart rate variability and evaluated which components, HF and/or LF, are affected compared with those of intermittent positive pressure ventilation (IPPV).

Method

Subjects

Nine patients (4 men and 5 women, aged 21–35 years) who were scheduled for elective orthopedic surgery participated in this study. The protocol had been approved by our institutional committee on research in humans. The subjects had no relevant medical history except for accidental trauma. They had fasted for at least 12 h prior to the study. Since some subjects were scheduled for afternoon surgery, a saline infusion ($2\,ml \cdot kg^{-1} \cdot h^{-1}$) was started at 8 A.M. through an 18-gauge catheter inserted into a right forearm vein.

Measurements

The subjects were instrumented and evaluated while in a supine position in the operating room. An electrocar-

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diogram was recorded via chest leads and a 22-gauge catheter was inserted into the left radial artery for direct measurement of arterial pressure (Life Scope 12, Nihon Koden, Tokyo, Japan) and for blood sampling. A contralateral 18-gauge catheter inserted into the left forearm vein prior to surgery was used to administer fluids and drugs. Partial pressures of arterial carbon dioxide ($Paco_2$) and oxygen (Pao_2) were measured with a blood gas analysis system (CIBA Corning 288 Blood Gas System, CIBA Corning Diagnostics, Medfield, MA, USA). All physiologic signals were transcribed onto FM tape and electrostatic paper recorders. Blood samples (7 ml), which were centrifuged immediately after withdrawal, and plasma were stored at −40°C for catecholamine assay (Special Reference Laboratory (SRL), Tokyo, Japan).

Experimental protocol

The experiment began after an initial 15-min resting period, during which the subject received an infusion of physiological saline. Anesthesia was induced with fentanyl ($10\,\mu g \cdot kg^{-1}$) and the subject was intubated endotracheally 5 min after the administration of vecuronium bromide $0.2\,mg \cdot kg^{-1}$. After tracheal intubation, the subject was initially ventilated with either IPPV or HFJV. The assigned order of the mode of ventilation was random, as determined by a coin toss. Four subjects received HFJV first. During IPPV, tidal volume was $8\,ml \cdot kg^{-1}$, the respiratory rate was 15 breaths·min^{-1}, and the inspiration/expiration ratio was 1:2 (Servo 900-C, Siemens-Elema AB, Solna, Sweden). During HFJV, the working pressure was $2.5\,kg \cdot (cm^2)^{-1}$ and the frequency was 5 Hz, with constant oxygen flow of $10\,l \cdot min^{-1}$ in the anesthetic circle. F_IO_2 was set at 1.0 during measurements. With each mode of ventilation, 5-min recordings were begun after hemodynamic stability had been achieved. Samples of arterial blood (7 ml) were collected at the end of each 5-min period of measurement for assay of catecholamines.

Data analysis

ECG, tidal volume, and arterial pressure waveforms were digitized at 1000 Hz with signal acquisition hardware and software (CODAS, Dataq Instruments, Akron, OH, USA) and stored on computer disk. Peak and volley analysis were performed to determine R-R intervals and systolic and diastolic arterial pressure.

Power spectral density was computed from the trendgram of 256 successive R-R intervals using a program for an autoregressive algorithm, according to the method described in detail by Hayano et al. [8]. In brief, the autoregressive coefficients were obtained by the Marple method [9]. The model order was the one that minimized Akaike's final prediction error figure of merit [10]. The provided center frequency and power were considered significant if those components contained more than 5% of the total power [11]. We defined the LF area as 0.05–0.15 Hz, and the HF area as 0.20–0.50 Hz.

Statistical analysis

Values are expressed as mean ± SE. The Wilcoxon test was used to compare all the physiological parameters and a level of $P < 0.05$ was considered to be statistically significant.

Results

Baseline values for each respiratory mode appear in Table 1. Mean R-R intervals, systolic and diastolic arterial pressure, $Paco_2$, and Pao_2 were similar during the two modes of respiration. Plasma norepinephrine and epinephrine both were significantly higher during HFJV than during IPPV.

Figure 1 shows recordings of the R-R interval and an analysis of the corresponding power spectral density during measurements. During IPPV there were two major components, the LF and the HF components at around 0.1 and 0.25 Hz, respectively. HF power was not detectable during HFJV, whereas the LF component persisted.

Figure 2 shows the statistical analysis of R-R interval power for the LF and HF areas. HF power was detected during IPPV (65.1 ± 14.3 ms^2), however, it was not detected in any subject during HFJV. There was no significant difference between IPPV and HFJV in LF power (108.8 ± 41.6 ms^2 *vs* 105.8 ± 22.4 ms^2).

Table 1. Baseline measurements for each respiratory mode

Parameter	IPPV	HFJV
mR-R (ms)	921 ± 50	968 ± 35
mSBP (mmHg)	147 ± 7	140 ± 8
mDBP (mmHg)	68 ± 3	63 ± 3
Nor (pg·ml^{-1})	369 ± 76	542 ± 84*
Epi (pg·ml^{-1})	659 ± 190	1114 ± 201*
$Paco_2$ (mmHg)	37 ± 2	36 ± 2
Pao_2 (mmHg)	538 ± 32	550 ± 24

Values are expressed as mean ± SE.
*$P < 0.05$ *vs* IPPV.
mR-R, mean R-R interva; mSBP, mean systolic blood pressure; mDBP, mean diastolic blood pressure; Nor, norepinephrine; Epi, epinephrine; IPPV, intermittent positive pressure ventilation; HFJV, high-frequency jet ventilation.

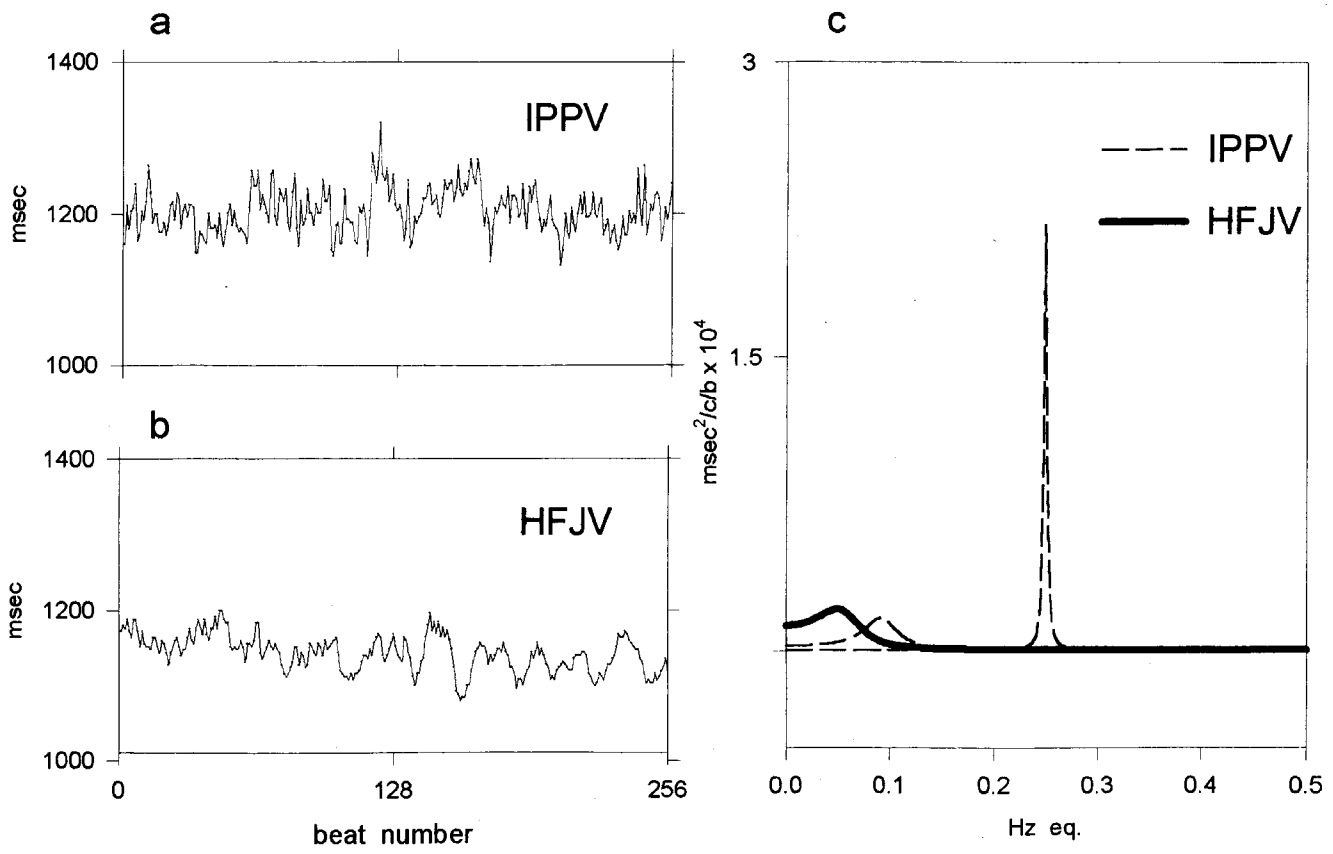

Fig. 1. Recording of 256 beats of R-R intervals (**a, b**) during measurements and analysis of their power spectrum (**c**) from one subject. *IPPV*, intermittent positive pressure ventilation; *HFJV*, high-frequency jet ventilation; *Hz eq*, frequency (Hz) equivalent

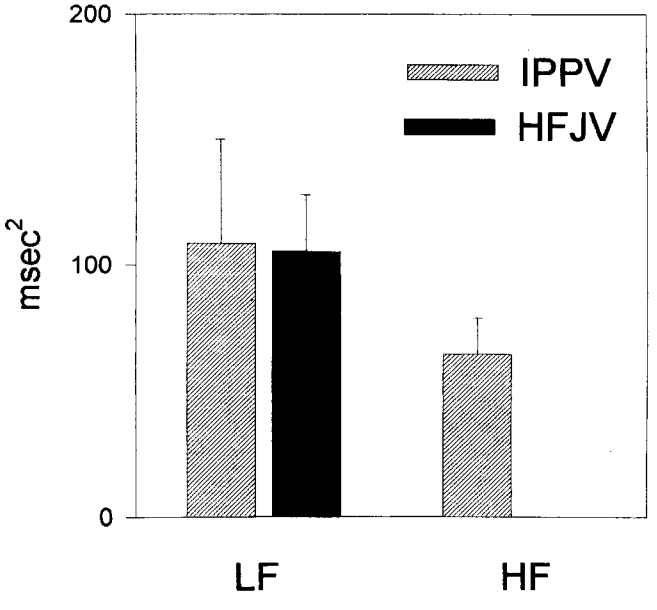

Fig. 2. Statistical analysis of R-R interval power. *Hatched bars* (*IPPV*), intermittent positive pressure ventilation; *solid bar* (*HFJV*), high-frequency jet ventilation; *LF*, low frequency; *HF*, high frequency

Discussion

This study shows the effect of HFJV on heart rate variability by use of power spectral density analysis. We found that during fentanyl anesthesia where heart rate and arterial pressure did not change, only HF power disappeared during HFJV, as compared with IPPV, whereas LF power remained the same. These data might imply that during fentanyl anesthesia, HFJV affects mainly the respiratory frequency heart rate variability without alteration in the net level of hemodynamic condition.

A previous study revealed that HFJV continuously stimulates pulmonary vagal afferent activity [4], causing an inhibition of reciprocal phrenic activity [5,6]. Eckberg [11] demonstrated that the human baroreflex response oscillates continuously during normal quiet breathing and that rapid breathing is associated with suppression of sinus arrhythmia and a loss of the differential responses to inspiratory and expiratory baroreceptor stimuli. It is generally assumed that the breathing pattern is the prime modulator of heart rate variability [11,12]. It seems logical, therefore, that the respiratory

drive from pulmonary and thoracic stretch receptors to bulbar respiratory motor neurons would be diminished during HFJV and would consequently cause a further decrease in neural input to the vagal cardiac nuclei within the range of respiratory frequencies, resulting in the disappearance of HF R-R interval power.

Clinical studies have shown that the return of venous blood from the peripheral vessels to the heart is greater during HFJV than during conventional ventilation [2,3]. However, during HFJV, the rhythmic fluctuation of venous return associated with respiration appears to be diminished. Consequently, the arterial pressure fluctuation associated with respiration apparently becomes smaller as well, which might result in a small amplitude of variability in the heart rate within the respiratory cycle [11].

Yet another possible mechanism for the diminished HF power is the effect of catecholamines. Our data showed that plasma concentrations of catecholamines were markedly elevated during HFJV. Sympathetic activation is generally associated with a decrease in heart rate variability [7]. Arai et al. observed that physical exercise drastically reduced both the LF and HF power of the R-R interval [14]. Pagani et al. [15] reported that the HF power of the R-R interval was slightly reduced by a hand-grip exercise, which was associated with an increased LF/HF ratio. Therefore, one would expect a reduction of the HF power during increased sympathetic activity.

The present study did not investigate arterial baroreflex regulation of heart rate during HFJV. Kotrly et al. [16] reported that fentanyl $10\mu g \cdot kg^{-1}$ reduced baroreflex-mediated tachycardia but maintained baroreflex-mediated bradycardia during combined anesthesia with diazepam and nitrous oxide. Rouby et al. [17] is the only group that has investigated the baroreflex during HFJV and compared it with conventional mechanical ventilation under fentanyl anesthesia. Those authors found that arterial baroreflex control of the heart rate after the induction of hypotension in response to nitroglycerin was higher during HFJV as compared with phenylephrine-induced hypertension, where no change was observed. The effect of high concentrations of catecholamine on arterial baroreflex control of heart rate is not known. Thus, a higher level of sympathetic outflow and a different baroreflex heart rate control via efferent vagal outflow during each of the two ventilation modes might influence the results.

The LF R-R interval power remained unchanged, despite an increase in the level of plasma catecholamines. The underlying mechanism for LF power is not known [18,19]. LF power is proposed as an index of sympathetic modulation [11]; however, when it is measured in the most straightforward way, LF does not respond to a variety of stimuli as one would expect of a pure measure of sympathetic tone [20,21]. Koh et al. [18] found that LF power was increased during the infusion of phenylephrine even in quadriplegic patients. No matter what the precise mechanism involved in this power, our results are difficult to interpret because of the presence of several variables, including fentanyl anesthesia, the administration of a muscle relaxant, the administration of mechanical ventilation, and an increase in the plasma concentration of catecholamines.

In conclusion, under hemodynamic conditions comparable to those of IPPV, HFJV reduced HF power so extensively that no peak was detected, whereas LF power remained unchanged instead of elevated plasma catecholamines. These data indicate that HFJV has a determinant effect on heart rate variability at around respiratory frequency, and that central mechanisms of attenuated neural input from the peripheral pulmonary and thoracic stretch receptors to the vagal cardiac nuclei might be involved. A further factor might be some combined effect of increased sympathetic nerve activity and fentanyl anesthesia.

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References

1. Carlon GC, Kahn RC, Howland WS, Ray C, Turnbull AD (1981) Clinical experience with high-frequency jet ventilation. Crit Care Med 9:1–6
2. Fusciardi J, Rouby JJ, Barakat T, Mal H, Godet G, Viars P (1986) Hemodynamic effects of high-frequency jet ventilation in patients with and without circulatory shock. Anesthesiology 65:485–491
3. Otto CW, Quan SF, Conaham JJ, Calkins JM, Waterson CK, Haneroff SR (1983) Hemodynamic effects of high-frequency jet ventilation. Anesth Analg 62:298–304
4. Kohl J, Koller EA (1984) Breathing pattern and stretch receptor activity during high-frequency ventilation. Pflügers Arch Eur J Physiol 402:150–156
5. Harrop-Griffiths AW, Chakrabarti MK, Whitman JG (1987) High-frequency ventilation and afferent vagal activity. Anesthesia 42:1162–1170
6. Man GCW, Man SFP, Kappagoda CT (1983) Effects of high-frequency oscillatory ventilation on vagal and phrenic activities. J Appl Physiol 54:502–507
7. Malliani A, Pagani M, Lombardi F, Cerutti S (1991) Cardiovascular neural regulation explored in the frequency domain. Circulation 84:482–492
8. Hayano J, Sakakibara Y, Yamada M, Mukai S, Fujinami T, Yokoyama K, Watanabe Y, Takata K (1991) Accuracy of assess-

ment of cardiac vagal tone by heart rate variability in normal subjects. Am J Cardiol 67:199–204
9. Marple L (1980) A new autoregressive spectrum analysis algorithm. IEEE Trans Acoust Speech Signal Processing ASSP-28:441–455
10. Akaike H (1969) Fitting autoregressive models for prediction. Ann Stat Math 21:234–247
11. Pagani M, Lombardi F, Guzzetti S, Rimoldi O, Furlan R, Pizzinelli P, Sandrone G, Malfatto G, Dell'Orto S, Piccaluga E, Turiel M, Baselli G, Cerutti S, Malliani A (1986) Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. Circ Res 59:178–193
12. Eckberg DL (1983) Human sinus arrhythmia as an index of vagal cardiac outflow. J Appl Physiol 54:961–966
13. Hirsch JA, Bishop B (1981) Respiratory sinus arrhythmia in humans: how breathing pattern modulates heart rate. Am J Physiol 241:H620–H629
14. Arai Y, Saul JP, Albreicht P, Hartley LH, Lilly LS, Cohen RJ, Colucci WS (1989) Modulation of cardiac autonomic activity during and immediately after exercise. Am J Physiol 256:H132–H141
15. Pagani M, Mazzuero G, Ferrari A, Liberati D, Cerutti S, Vaitl D, Tavazzi L, Malliani A (1991) Sympathovagal interaction during mental stress. Circulation 83[Suppl II]:II-43–II-51
16. Kotrly KJ, Ebert JJ, Vucins EJ, Roerig DL, Stadnicka A, Kampine JP (1986) Effects of fentanyl-diazepam-nitrous oxide anesthesia on arterial baroreflex control of heart rate in man. Br J Anesth 58:406–414
17. Rouby JJ, Houissa M, Brichant JF, Baron JF, McMillan C, Arthaud M, Amzallag P, Viars P (1987) Effects of high-frequency jet ventilation on arterial baroreflex regulation of heart rate. J Appl Physiol 63:2216–2222
18. Koh J, Brown TE, Beightol LA, Ha CY, Eckberg DL (1994) Human autonomic rhythms: vagal cardiac mechanisms in tetraplegic subjects. J Physiol (London) 474(3):483–495
19. Inoue K, Miyake S, Kumashiro M, Ogata H, Yoshimura O (1990) Power spectral analysis of heart rate variability in traumatic quadriplegic humans. Am J Physiol 258:H1722–H1726
20. Saul JP, Rea RF, Eckberg DL, Berger RD, Cohen RJ (1990) Heart rate and muscle sympathetic nerve variability during reflex changes of autonomic activity. Am J Physiol 258:H713–H721
21. Hopf HB, Skyschally A, Heusch G, Peters J (1995) Low-frequency spectral power of heart rate variability is not a specific marker of cardiac sympathetic modulation. Anesthesiology 82:609–619