RESPIRATORY SINUS ARRHYTHMIA: A NEW, OBJECTIVE SEDATION SCORE

D. Y. WANG, C. J. D. POMFRETT AND T. E. J. HEALY

SUMMARY

We tested if microcomputer-based measurements of heart rate variability and respiratory sinus arrhythmia (RSA) could be used as the basis of an objective sedation score. Measurements were obtained in eight ICU patients before, during and after physiotherapy. Patients were sedated with propofol and alfentanil and paralysed with atracurium. Mean ECG R-R interval showed little variation, changing from 646.15 (SD 203.15) ms to 596.08 (181.75) ms and 633.98 (184.53) ms before, during and after physiotherapy, respectively (not significant). However, the degree of respiratory sinus arrhythmia, determined using circular statistical analysis, increased significantly, from 0.14 (0.11) to 0.24 (0.15), during physiotherapy and returned to control after physiotherapy (P < 0.05). Changes in respiratory sinus arrhythmia may provide an objective measurement of sedation in ICU patients and could form the basis of a simple sedation scoring system. (Br. J. Anaesth. 1993; 71: 354-358)

KEY WORDS
Heart: respiratory sinus arrhythmia. Measurement techniques: heart rate variability, sedation.

Cardiac beat-to-beat variability (R-R variability) is a non-pathological feature of most normal ECG records, and is especially pronounced in children and young adults. The most consistent feature of heart rate variability is respiratory sinus arrhythmia (RSA), in which the heart rate increases during inspiration and decreases during expiration, through a predominately parasympathetic reflex connecting stretch receptors in the lungs and aorta to vagal motor neurones innervating the heart. Wheeler and Watkins [1] reported that there was a reduction in heart rate variability in diabetic patients exhibiting autonomic neuropathy associated with vagal denervation of the heart. Subsequent reports [2-4] confirmed that heart rate variability could be used as a clinical test in the diagnosis of diabetic peripheral neuropathy. Donchin, Feld and Porges [5] used an off-line technique to observe changes in RSA in 10 female patients during isoflurane-nitrous oxide anaesthesia, and suggested that on-line analysis of RSA might provide a physiological index of depth of anaesthesia and rate of recovery. Sakuma, Ueda and Kiode [6] investigated heart rate variability and the function of the autonomic nervous system during general anaesthesia in 26 patients, and further concluded that heart rate variability might provide information which could be useful for monitoring depth of anaesthesia. However, the previous reports collected data over prolonged periods, such as 10 min, and have, therefore, had only low temporal resolution. This is undesirable in any putative indicator of anaesthetic depth. In addition, the earlier reports did not use real time, on-line analysis during anaesthesia, which would be required for a patient monitoring system, but depended instead on off-line analysis. Pomfrett and colleagues [7] reported changes in RSA, using on-line analysis, observed during general anaesthesia in 60 patients. Reductions in RSA during anaesthesia, together with increases in RSA during the recovery period, were identified. These results suggested that RSA, analysed on-line, may also be a useful indicator of depth of anaesthesia.

The majority of patients in the ICU are sedated and it would be useful to have an objective measurement system which could identify if sedation is either too profound or inappropriately light. The ideal system would also be simple, and able to present sedation scores to ICU staff in real-time, as a result of on-line analysis. The present study was designed to evaluate if changes in both heart rate variability and RSA could form the basis of a monitor for assessing depth of sedation in patients during intensive care, in order to develop a simple, objective sedation score.

PATIENTS AND METHODS

Informed consent was obtained from ICU patients or relatives of patients, in accordance with a research proposal approved by our local Ethics Committee. All the patients were paralysed with atracurium and sedated with propofol and alfentanil, which were infused constantly through infusion pumps (see table I for dosage). Drug administration was maintained...
performed on all the patients by the same physiotherapist. Data were collected continuously from 15 min before physiotherapy until 15 min after physiotherapy concluded. Heart rate, core temperature and arterial $P_{\text{CO}_2}$ were measured using standard ICU monitors.

A microcomputer-based data logging system was used to collect ECG and respiratory data, using multi-tasking software developed for the study. Details of the equipment have been published elsewhere [8]. The ECG was collected using isolated research amplifiers (Digitimer Neurolog). A turbine-based flowmeter (FDE Magtrak) was introduced into the breathing circuit and gave a pulse train during inspiration. The ECG was amplified to ±5 V peak-to-peak amplitude and then digitized to 12-bit, 1-KHz accuracy, using a programmable laboratory interface (CED 1401). Ventilatory pulses were logged as events to 1 ms accuracy by the interface and both signals were uploaded to microcomputer (Acorn Archimedes RISC workstation) for on-line analysis and archiving of raw data.

The degree of RSA was determined using a modified version of the mean circular resultant technique described for screening diabetics exhibiting autonomic neuropathy [9] (fig. 1). The principal modification was that patients were not able to maintain a fixed duration of breathing cycle, and so successive ventilatory cycles were normalized online and in real-time by a computer program designed for this study. Each complete cycle of inspiration and expiration was normalized, so that it began at 0° and ended at 359°, irrespective of its duration. ECG R-wave times were logged as individual vectors within each ventilatory cycle, with magnitude 1 and angle dependent on the position in the cycle. For example, an ECG R-wave occurring at the midpoint of the ventilatory cycle would be represented by a vector with an angle of 180° and a magnitude of 1. The following variables were obtained (fig. 1):

- $R$: the mean vector length of several vectors of the ECG R-waves recorded during a 30-s epoch. The magnitude of each mean vector describes the degree of clustering of the R-wave distribution within a ventilatory cycle, and hence the degree of RSA. The range of its value is from 0 to 1.
- $P$: the 0.05 probability level for Rayleigh’s test of randomness [10]. If $R$ exceeds $P$, there is a significant increase in the amount of clustering of the ECG R-waves within a ventilatory cycle and, therefore, an increase in the degree of RSA.
- $\theta$: the mean vector angle of several vectors of ECG R-waves. $\theta$ denotes the position of the mean of the ECG R-wave cluster within a ventilatory cycle. This effectively denotes the phase of RSA during ventilation.

Mean angular deviation: this is the circular statistical analogue of the linear $\text{SD}$, and indicates the distribution of R vector angles about the mean R vector angle. Constant for at least 2 h before the start of data collection and no additional doses were given before or during the data collection period. The patient’s tracheas were intubated and their lungs ventilated during the study. Physiotherapy was used as a standardized stimulation and consisted of “bag squeezing” (manual hyperinflation of the lungs), massage of the chest, suction and passive movement of the upper and lower limbs. The procedures were

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Fig. 1. Derivation of indices describing respiratory sinus arrhythmia (RSA). This schematic diagram follows the structured design of on-line, multi-tasking software developed by CJDJP. A: The raw ECG was digitized at 1-KHz, R-waves were discriminated using an analog pulse trigger (threshold shown by dotted line) and the resulting R-wave pulses logged as events with timings relative to the start of each computer data file. Pulses from a flowmeter were also logged as events to 1 ms accuracy. Arrows denote the beginning of each inspiration. B: The computer determined the onset of each inspiration from the pattern of ventilatory pulses. Occasional isolated pulses (*) caused by mechanical movement of the flowmeter were rejected by the computer. The ECG R-wave event pulses were then time-normalized relative to the beginning of each ventilatory cycle. Arrow denotes the onset of inspiration, the duration of which is marked by the solid bar. C: Normalized ECG R-wave times were converted into vector co-ordinates, with a magnitude of 1 and an angle dependent on the position in the ventilatory cycle (e.g. an ECG R-wave at the onset of inspiration would have an angle of 0° and a magnitude of 1, whereas an R-wave exactly halfway through the ventilatory cycle would have an angle of 180° and a magnitude of 1). Filled bar denotes inspiration. D: Vectors were plotted together for successive ventilatory cycles, and a mean vector calculated. The mean vector length ($R$, shown × 10 on the figure) was proportional to the amount of clustering of the ECG R-waves relative to inspiration, and gave an indication of RSA. The mean vector angle ($\theta$) was also calculated. Mean angular deviation (MAD) was the circular analogue of a linear $\text{SD}$ and indicates the distribution of vector angles about the mean vector angle.
TABLE I. Patient characteristics and drug therapy (mean (range or SD))

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>No. of patients</td>
<td>8</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>46.8 (23-78)</td>
</tr>
<tr>
<td>Outcome (survived/died)</td>
<td>6/2</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>5/3</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>75.9 (15.73)</td>
</tr>
<tr>
<td>Propofol (mg kg(^{-1}) h(^{-1}))</td>
<td>1.55 (0.65)</td>
</tr>
<tr>
<td>Alfentanil ((\mu)g kg(^{-1}) h(^{-1}))</td>
<td>6.91 (1.92)</td>
</tr>
<tr>
<td>Atracurium (mg kg(^{-1}) h(^{-1}))</td>
<td>0.79 (0.24)</td>
</tr>
</tbody>
</table>

index of heart rate variability [11], and contains RSA as a component. It is presented in this study in order to provide a common reference against previous studies.

All the data in the three periods (before, during and after physiotherapy) were compared using ANOVA (analysis of variance). Data files were copied onto an IBM AT-compatible computer and analysed using standard software [12]. \(P < 0.05\) was considered significant.

TABLE II. Cardiovascular response and heart rate variability (mean (SD)). MAD = Mean angular deviation. \(^*P < 0.05\) (ANOVA)

<table>
<thead>
<tr>
<th></th>
<th>Before physiotherapy</th>
<th>During physiotherapy</th>
<th>After physiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>(R)</td>
<td>0.14 (0.11)</td>
<td>0.24 (0.15)*</td>
<td>0.15 (0.13)</td>
</tr>
<tr>
<td>(P)</td>
<td>0.34 (0.04)</td>
<td>0.36 (0.03)</td>
<td>0.35 (0.03)</td>
</tr>
<tr>
<td>(\theta) ((^\circ))</td>
<td>172.93 (32.04)</td>
<td>174.11 (28.92)</td>
<td>175.03 (26.14)</td>
</tr>
<tr>
<td>MAD ((^\circ))</td>
<td>75.01 (4.46)</td>
<td>70.47 (6.44)*</td>
<td>74.47 (5.04)</td>
</tr>
<tr>
<td>R–R interval (ms)</td>
<td>644.15 (203.15)</td>
<td>596.08 (181.75)</td>
<td>653.98 (184.53)</td>
</tr>
<tr>
<td>SD of R–R interval (ms)</td>
<td>29.97 (24.80)</td>
<td>79.06 (100.48)*</td>
<td>21.97 (23.43)</td>
</tr>
<tr>
<td>Heart rate (beat min(^{-1}))</td>
<td>93.20 (6.70)</td>
<td>100.30 (5.80)</td>
<td>94.64 (5.90)</td>
</tr>
<tr>
<td>Mean AP (mm Hg)</td>
<td>97.20 (6.90)</td>
<td>106.90 (6.10)*</td>
<td>96.44 (5.30)</td>
</tr>
</tbody>
</table>

**RESULTS**

We studied eight patients; two subsequently died in the ICU and six were discharged to the wards. Patient characteristics and some clinical data are shown in table I.

The changes in heart rate variability, derived parameters and haemodynamic variables are shown in table II. \(R\) increased significantly \((P < 0.01)\), from 0.14 to 0.24—an increase of 71 \(\%\) during the period of physiotherapy. Figure 2 shows the changes in \(R\) from a single patient during physiotherapy. Mean ECG R–R interval decreased slightly, from 646.15 ms to 596.08 ms (8.0 \(\%\)), during physiotherapy (not significant). The SD of the ECG R–R interval increased from 29.97 ms to 79.06 ms (163.8 \(\%\)) during physiotherapy \((P < 0.05)\) and returned to the initial value after physiotherapy. The \(P\) value of Rayleigh's test, \(\theta\) and the mean angular deviation remained unchanged during physiotherapy \((P > 0.05)\).

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**Fig. 2.** ARIMA (Auto Regressive Integrated Moving Average) analysis of the circular statistical index of RSA \((R)\) against time before, during and after physiotherapy for one patient. Upper \((-\cdots-\cdots\cdots)\) and lower \((-\cdots-\cdots\cdots)\) 99 \(\%\) confidence intervals are shown, showing the predicted deviation from \(R\) (ARIMA \((R)\)) based on the behaviour of \(R\) before physiotherapy. \(R\) increased to significantly greater than ARIMA \(R\) during physiotherapy, and decreased back to the predicted, ARIMA, \(R\) value again after physiotherapy was completed. \(R\) decreased after the change to manual ventilation (MV) but this decrease did not exceed the 99 \(\%\) confidence interval for ARIMA \(R\). SP = Start of physiotherapy; EP = end of physiotherapy.
Both heart rate and mean arterial pressure, taken from standard ICU monitors, increased during physiotherapy and returned to previous values after physiotherapy; changes in mean arterial pressure were significant ($P < 0.05$) but those in heart rate were not. No significant differences were observed in core temperature or arterial $P_{CO_2}$ either between patients or during the course of individual recordings.

**DISCUSSION**

It has been suggested that the degree of sedation in ICU patients should be measured as routinely as ECG and arterial pressure [13], but there appears to be no objective method available. Existing scoring systems are based on subjective estimates of level of sedation, making them potentially unreliable, time-consuming and generally unsuitable for routine use in a busy ICU.

Our data suggest that changes in heart rate variability and RSA during physiotherapy are related to changes in degree of sedation in patients in the ICU. The magnitude of RSA ($R$) increased during the period of physiotherapy compared with baseline obtained during the period before physiotherapy. This finding is similar to that reported elsewhere during lightening of general anaesthesia. Donchin, Feld and Porges [5] reported an increase in heart rate variability during recovery from isoflurane-nitrous oxide anaesthesia. Pomfrett and colleagues [7] studied the changes in RSA in 60 patients undergoing elective surgery and showed an increase in RSA both after tracheal intubation and during recovery from anaesthesia.

The changes in heart rate variability observed in the present study reflect an increase in activity in the autonomic nervous system during physiotherapy, although the patients were sedated with propofol and alfentanil and paralysed with atracurium. Yama-mura, Tomomasu and Furukawa [14] observed that halothane depressed vagal tone by up to 30% of control in cats and that this reduction was dose-dependent. The mechanism of this depression is affected by many factors [6], the most important of which is depression of the respiratory and cardiovascular centres. Most anaesthetic agents depress activity in these centres, which leads to changes in breathing pattern and cardiovascular indices. When the vagal influence on the heart is blocked or attenuated during anaesthesia, heart rate variability tends to be reduced. This variation can be recognized in both anaesthetized and sedated patients. It is likely that arousal caused by physiotherapy results in an increase in brain activity, leading to an increase in vagal tone and changes in heart rate variability.

We used circular statistical analysis to enable changes in $R$–$R$ interval caused by RSA to be isolated from other causes. This is particularly useful for patients in the ICU, many of whom suffer from haemodynamic changes which cause arrhythmias in addition to RSA. In order to compare the sensitivity of linear and circular statistical analysis in detecting heart rate variability, the recordings were analysed using both methods. The results showed that circular statistics were more appropriate than linear statistics for quantifying RSA. During physiotherapy, the changes in $R$, calculated using circular statistics, increased significantly, by 71%, compared with baseline values before physiotherapy. However, the mean $R$–$R$ interval was only 7% shorter during physiotherapy than that observed before physiotherapy, and the change was not significant. The increase in $\sigma$ from the mean ECG $R$–$R$ interval during physiotherapy was 264%. This suggests that other, non-ventilatory factors had a substantial influence on the heart rate during physiotherapy. For example, the $\sigma$ of the heart rate has been shown to be linked to intrinsic heart rate, affected by changes in average heart rate, and pre-ventricular contractions [15], whereas $R$ is only minimally affected by pre-ventricular contractions and is not affected by changes in either average or intrinsic heart rate.

We also observed a small, but insignificant, change in $\theta$ during measurement of heart rate variability. $\theta$ is the mean angle of several individual ECG R-wave vectors and denotes the phase of RSA within the ventilatory cycle. During physiotherapy, $\theta$ was 8% greater than baseline and remained increased after physiotherapy. However, the changes were not statistically significant.

For use as a sedation score, the on-line trended record of RSA would be observed by ICU staff, especially preceding potentially stimulating procedures. Significant increases in $R$ could then be followed by appropriate increases in the rate of sedative infusion. We are currently investigating methods of implementing on-line monitoring of RSA as the basis of a sedation scoring system, and the results of these studies will be the subject of further communications.

**ACKNOWLEDGEMENTS**

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