Respiratory sinus arrhythmia: opposite effects on systolic and mean arterial pressure in supine humans

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1. Are arterial blood pressure fluctuations buffered or reinforced by respiratory sinus arrhythmia (RSA)? There is still considerable debate about this simple question. Different results have been obtained, triggering a discussion as to whether or not the baroreflexes are responsible for RSA. We suspected that the measurements of different aspects of arterial pressure (mean arterial pressure (MAP) and systolic pressure (SP)) can explain the conflicting results.

2. Simultaneous recordings of beat-to-beat MAP, SP, left cardiac stroke volume (SV, pulsed ultrasound Doppler), heart rate (HR) and respiration (RE) were obtained in 10 healthy young adults during spontaneous respiration. In order to eliminate HR variations at respiratory frequency we used propranolol and atropine administration in the supine and tilted positions. Respiration-synchronous variation in the recorded variables was quantified by spectral analysis of the recordings of each of these variables, and the phase relations between them were determined by cross-spectral analysis.

3. MAP fluctuations increased after removing heart rate variations in both supine and tilted position, whereas SP fluctuations decreased in the supine position and increased in the head-up tilted position.

4. RSA buffers respiration-synchronous fluctuations in MAP in both positions. However, fluctuations in SP were reinforced by RSA in the supine and buffered in the tilted position.

The relationship between RSA and respiration-synchronous variation in arterial blood pressure is still under discussion. RSA is caused by changes in vagal impulse traffic at resting respiratory frequency (Saul & Cohen, 1994).

Variations in arterial blood pressure may be caused by variations in total peripheral resistance (TPR) or in cardiac output (CO). At the respiratory frequency, the sympathetic nerves controlling the peripheral arteries do conduct the rapid changes in arterial blood pressure, but these changes need a certain time to develop fully over the synapse and to obtain a fully contracting effect on the smooth muscles in the arterial wall (Toska et al. 1994). This leaves us with fluctuations in CO to explain the respiration-synchronous blood pressure variations. Cardiac output variability is caused by variations in HR and SV: CO = HR × SV.

Thus, respiration-synchronous blood pressure variations could be caused by HR variations. If this is the case, they would vanish or be weakened after the administration of atropine. Blood pressure variance may also be caused by SV variations. If the respiration-synchronous blood pressure variations were reinforced by SV variations and weakened by HR variations, they would increase after atropine administration, since atropine eliminates HR variations. In a previous study from our group, this was found to happen and taken to mean that HR variations buffer blood pressure variations at respiratory frequency (Toska & Eriksen, 1993). In contrast, a recent study by Taylor & Eckberg (1996) showed a decrease in respiration-synchronous blood pressure variations after removal of heart rate variations, and concluded that respiratory HR variations contributed to blood pressure fluctuations.

However, the two studies were not entirely comparable, because Toska & Eriksen (1993) recorded MAP whereas Taylor & Eckberg (1996) recorded SP and diastolic pressure (DP). In clinical practice we are used to referring to SP and DP since these are what we measure with a
sphygmomanometer. With continuous measurements of arterial pressure it is possible to integrate MAP into the analysis.

In order to test the influence of methodological differences we analysed respiration-synchronous variations in MAP and SP both before and after medication, in addition to the variations in HR, SV and CO both in the supine position and in a 30 deg head-up tilt position (Taylor & Eckberg, 1996; Sloan et al. 1997).

METHODS

Subjects

Ten healthy volunteers – five males and five females – were studied (age, 25.2 ± 3.7 years (mean ± s.d.); height, 170.3 ± 8.6 cm; weight, 68.2 ± 8.4 kg). All subjects were non-smokers and none was taking any medication. Written informed consent was obtained from all participants, and the experimental protocol was approved by the Massachusetts Institute of Technology Committee on the Use of Humans as Experimental Subjects. All experiments were performed at the Clinical Research Center, Massachusetts Institute of Technology. All experiments conformed with the Declaration of Helsinki.

Experimental design

This investigation was part of a more extensive study, which explains why parts of the protocol are not relevant to the present investigation. Cardiovascular recordings were obtained before, during and after medication on two different experimental days. On one day, the subjects were tested in the supine position before and after administration of first propranolol and then atropine. On another day, we administered first atropine and then propranolol, and tested in a 30 deg head-up tilted position. In randomized order, four subjects were tested in the supine position on the first day and six in the tilted position.

On the supine day, the recordings started with a head-down tilt for 15 min, followed by recording in a supine position, which we from now on will refer to as the ‘supine control state’. After propranolol was injected in the supine position, recordings were made in the supine position. Then atropine was injected, followed by further recordings in the supine position.

On the tilt day, the recordings started with the subject in the supine position, followed by recording in the tilted position, referred to as the ‘tilted control state’. After atropine was injected in the supine position, a recording was made in the tilted position.

In each position, the recording included 5 min of spontaneous breathing. In this analysis we have used recordings made during spontaneous breathing from both test days, but only those made in the supine and the tilted control states and those made immediately after atropine administration on both days.

Instrumentation

Respiration (RE) was measured by two-belt chest–abdomen inductance plethysmography (Respitrace System, Ambulatory Monitoring Systems, Ardsley, NY, USA). The equipment was calibrated before each recording session by having the subjects alternately fill and empty an 800 ml Spirobag.

Beat-to-beat SV was recorded using an ultrasound Doppler method (Eriksen & Walløe, 1990). A bi-directional ultrasound Doppler velocimeter (CFM 750, GE Vingmed, Horten, Norway) was operated in pulsed mode at 2 MHz, with the hand-held transducer at the suprasternal notch. In a separate session, the diameter of the rigid aortic ring was determined by parasternal sector-scanner imaging (CFM 750, GE Vingmed, Horten, Norway). On the assumption that the orifice is circular, this diameter was used to calculate the area of the aortic valvular orifice. SV was calculated by multiplying the value obtained by numerical integration of the recorded instantaneous maximum velocity during each R–R interval by the area of the orifice. This calculation is based on the assumption that the velocity profile in the aortic valvular orifice is rectangular, and this that velocity is conserved as the central maximum velocity of a jet 3–4 cm upwards in the aortic root (Eriksen & Walløe, 1990).

Instantaneous HR was obtained from the duration of each R–R interval of the ECG signal, and beat-to-beat CO was calculated from the corresponding HR and SV values.

Finger arterial pressure was recorded continuously (2300 Finapres BP monitor, Ohmeda, Madison, W1, USA). The instantaneous pressure output was transferred on-line to the recording computer and beat-to-beat MAP was calculated by numerical integration. Beat-to-beat SP was the highest pressure during each R–R interval. Arterial pressure obtained by this method has been shown to be in good accordance with central, intra-arterial pressure in various situations (Parati et al. 1989; Imholz et al. 1990).

All signals were transferred on-line to a recording computer running a dedicated data collection and analysis program (program for real data acquisition: Morten Eriksen, Oslo, Norway).

Medication

The subjects received 14.6 mg propranolol and 0.04 mg kg⁻¹ atropine (Saul et al. 1991; Toska & Eriksen, 1993).

Mathematical and statistical analysis

From each recording we selected a continuous sequence where recording of all variables was technically successful. Parts of the recordings in one subject in the supine control state and after propranolol and atropine administration are shown in Fig. 14. The sequences selected for analysis were ~5 min. One subject (No. 10) had four supra-ventricular extra systoles on the tilt day and 11 on the supine day, which were removed before analysis. This subject is included in all statistical calculations. The power spectra of the selected time series were then calculated by fast Fourier transform. Examples of power spectra from one subject in the supine control state and after propranolol and atropine administration are shown in Fig. 1B. From the power spectra we calculated the integral under the curve in an interval of bandwidth 0.15 Hz, and this was used as an estimate of variance at the respiratory frequency. The peak of the respiratory frequency varied individually between 0.16 Hz and 0.37 Hz, and to cover the respiratory variance, we moved the interval according to the peak of the respiration power spectra. In our analysis we have quantified the frequency-specific variations with absolute values. In addition, we performed the analysis using the variation coefficients and found no significant difference between the statistical results of the two methods.

Phase angles and coherence between RE and all cardiovascular variables were obtained from the cross-spectra at the peak respiratory frequency (Fig. 2). Average phase angles were computed by weighting the phase angles with their squared coherence.

The statistical significance of changes was tested by the Wilcoxon signed rank sum test. $P < 0.05$ was considered significant.
Figure 1. Recordings and the power spectra of the variables

A shows a small part of the recorded variables from one subject in the supine control state and after propranolol and atropine administration. The x-axes show time in seconds, and for each variable the range of the y-axis is kept constant to compare fluctuations in the supine control state and after medication. B shows the power spectra from one subject in the supine control state and after medication. The x-axes show frequency in hertz. The variance was calculated as the integral under the curve in an interval of bandwidth 0.15 Hz moved according to the respiration peak. After medication, HR increases and RSA is almost eliminated. SV decreases after medication, and there are fewer fluctuations at respiratory frequency. CO increases and its fluctuations increase at respiratory frequency after medication. After medication, MAP increases and the oscillations at respiratory frequency increase. SP increases after medication and its fluctuations at respiratory frequency decrease. RE, respiration; HR, heart rate; SV, stroke volume; CO, cardiac output; MAP, mean arterial pressure; SP, systolic pressure; REvar, variance in respiration; HRvar, variance in HR; SVvar, variance in SV; COvar, variance in CO; MAPvar, variance in MAP; SPvar, variance in SP.
RESULTS

Propranolol and atropine administration

Table 1 summarizes mean values of RE, HR, SV, CO, MAP and SP and their mean variances at respiratory frequency in the control state and after medication on the supine and tilt days.

Neither variance in RE nor peak respiratory frequency changed after medication in the supine or tilted position. Variance in HR decreased on both test days (Fig. 3A and B; \( P = 0.001 \)).

Table 2 shows the average phase lags between RE and all cardiovascular variables in the supine position at peak

Variance and phase at respiratory frequency in the supine position

Figure 3B illustrates variance in the variables in the supine control state and after propranolol and atropine administration. Variance in SV decreased (\( P = 0.005 \)), while variance in CO increased (n.s., \( P = 0.053 \)). Variance in MAP increased after medication (\( P = 0.001 \)), while variance in SP decreased (\( P = 0.032 \)).

Table 2 shows the average phase lags between RE and all cardiovascular variables in the supine position at peak

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Table 1. Mean values (± S.D.) and mean variance in the supine and tilted positions

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<thead>
<tr>
<th></th>
<th>Supine position</th>
<th>Tilted position</th>
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<tbody>
<tr>
<td></td>
<td>Control state</td>
<td>After medication</td>
</tr>
<tr>
<td>RE (breaths min⁻¹)</td>
<td>15.3 ± 3.2</td>
<td>15.8 ± 2.3</td>
</tr>
<tr>
<td>HR (beats min⁻¹)</td>
<td>55 ± 9</td>
<td>96 ± 19*</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>101 ± 12</td>
<td>81 ± 13*</td>
</tr>
<tr>
<td>CO (l min⁻¹)</td>
<td>5.5 ± 1.0</td>
<td>7.7 ± 1.2*</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>79 ± 8</td>
<td>119 ± 24*</td>
</tr>
<tr>
<td>SP (mmHg)</td>
<td>121 ± 16</td>
<td>163 ± 25*</td>
</tr>
<tr>
<td>DP (mmHg)</td>
<td>63 ± 8</td>
<td>99 ± 21*</td>
</tr>
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</table>

At respiratory frequency:

<table>
<thead>
<tr>
<th></th>
<th>Supine position</th>
<th>Tilted position</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Control state</td>
<td>After medication</td>
</tr>
<tr>
<td>REvar (l²)</td>
<td>0.013</td>
<td>0.013</td>
</tr>
<tr>
<td>HRvar (beats min⁻¹²)</td>
<td>5.493</td>
<td>0.066*</td>
</tr>
<tr>
<td>SVvar (ml²)</td>
<td>22.79</td>
<td>7.487*</td>
</tr>
<tr>
<td>COvar (l min⁻¹²)</td>
<td>0.045</td>
<td>0.07</td>
</tr>
<tr>
<td>MAPvar (mmHg²)</td>
<td>0.266</td>
<td>0.54*</td>
</tr>
<tr>
<td>SPvar (mmHg²)</td>
<td>1.816</td>
<td>1.092*</td>
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</tbody>
</table>

* Significantly different (\( P < 0.05 \)) from supine control state. † Significantly different (\( P < 0.05 \)) from tilted control state. Abbreviations as in Fig. 1.

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Figure 2. Cross-spectral analysis

The panels show parts of the cross-spectral analysis in the same subject as in Fig. 1 in supine control state. The x-axes show frequency in hertz. A shows, from the top, phase between HRvar and REvar, coherence between HRvar and REvar, HRvar and REvar. B shows, from the top, phase between MAPvar and REvar, coherence between MAPvar and REvar, MAPvar and REvar. The phase was read at the peak respiratory frequency. Note that the coherence reaches a maximum value at the respiratory peak frequency in both HRvar and MAPvar. Abbreviations as in Fig. 1.
respiratory frequency. Figure 4A illustrates the phase angles between RE and the cardiovascular variables in the supine control state, and Fig. 4B illustrates the situation after medication. Changes in RE and HR are in phase in the supine control state, whereas changes in CO, SV, SP and MAP are inversely related to changes in RE. After medication, changes in RE and HR are no longer in phase, and the changes in the other variables are more clustered and in inverse phase with RE.

**Variance and phase at respiratory frequency in the tilted position**

Figure 3A illustrates variance in the variables in the tilted control state and after atropine administration. Variance in SV decreased (n.s., $P = 0.08$), and variance in CO increased ($P = 0.005$). Variance in MAP and SP increased ($P = 0.002$ and $P = 0.024$).

The average phase lags in the tilted position are summarized in Table 2. Figures 4C and D illustrate the phase angles in the tilted control state and after atropine administration, respectively. In the tilted control state, changes in RE and HR are in phase, whereas the changes in the other variables are in inverse phase. After atropine administration, the phase angle relationships are very similar to those in the supine position after medication. Changes in RE and HR are no longer in phase, and the changes in the other variables are more clustered and in inverse phase.

**DISCUSSION**

Our most important finding is that in the supine position, the respiration-synchronous variability in MAP increases, whereas the variability in SP decreases when HR variations are eliminated. Thus RSA buffers MAP variations in the supine position, but increases variations in SP. This explains why differing conclusions have been reached in previous publications where MAP and SP were compared (Toska & Eriksen, 1993; Taylor & Eckberg, 1996). In the tilted position, variations in both MAP and SP increase at respiratory frequency after HR variability is eliminated, showing that in the tilted position RSA buffers variations in both MAP and SP.

This study confirms that RSA plays a role in buffering mechanically induced variations in CO and MAP during respiration (Toska & Eriksen, 1993).

**Relationship between HR and SV in the supine position**

Figure 1 clearly illustrates our general finding of an inverse relationship between HR and SV. The phase between HR and SV was approximately 160 deg in the supine position (Fig. 4A) at the respiratory frequency. This means that, when there is an increase in HR, there is

![Figure 3. Variance in HR, SV, CO, MAP and SP](image)

**Table 2. Phase lag between RE and other variables in the supine and tilted positions**

<table>
<thead>
<tr>
<th></th>
<th>Supine position</th>
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<th>Tilted position</th>
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<tbody>
<tr>
<td></td>
<td>Control state</td>
<td>After medication</td>
<td>Control state</td>
<td>After atropine</td>
</tr>
<tr>
<td>RE cycle (s)</td>
<td>3.92</td>
<td>3.80</td>
<td>3.51</td>
<td>3.75</td>
</tr>
<tr>
<td>RE–HR (s)</td>
<td>0.13</td>
<td>1.22</td>
<td>0.06</td>
<td>1.31</td>
</tr>
<tr>
<td>RE–CO (s)</td>
<td>1.37</td>
<td>2.36</td>
<td>1.47</td>
<td>2.39</td>
</tr>
<tr>
<td>RE–SV (s)</td>
<td>1.80</td>
<td>2.40</td>
<td>1.62</td>
<td>2.40</td>
</tr>
<tr>
<td>RE–SP (s)</td>
<td>2.08</td>
<td>2.67</td>
<td>1.72</td>
<td>2.57</td>
</tr>
<tr>
<td>RE–MAP (s)</td>
<td>2.42</td>
<td>2.50</td>
<td>1.84</td>
<td>2.36</td>
</tr>
</tbody>
</table>

Values are coherence-weighted means expressed as appearance in the respiration cycle in seconds after start of inspiration. Abbreviations as in Fig. 1.
a decrease in SV, as seen during inspiration. Thus RSA buffers respiration-induced fluctuations in CO.

After propranolol and atropine administration, variations in HR were almost eliminated and CO variations increased considerably. Even though the variations in SV decreased after medication, the impact of the SV variations on CO increased in the absence of buffering HR variations.

HR rises in the supine control state when or even before inspiration starts (Saul et al. 1989, 1991) (Table 2 and Fig. 4A). This change appears so quickly as to suggest central feedforward control (Saul & Cohen, 1994). Since a reflex loop requires ~0.25 s to develop (Borst & Karemaker, 1983), any HR changes elicited by the arterial baroreceptors could not appear as quickly as the observed HR variations. From this we conclude that impulses from the arterial baroreceptors cannot be the only cause of RSA. After medication, the small changes in HR that persist follow later in the respiration cycle (Saul et al. 1991). Assuming total muscarinic and β-adrenoreceptor blockade of the heart, these small changes are probably due to an intracardiac reflex or mechanical stretching of the sinoatrial node (Saul & Cohen, 1994). These variations in HR are not large enough to have any impact on CO variations. As a result, CO and SV variations after medication follow each other closely during the respiratory cycle (Table 2 and Fig. 4B).

**Relationship between HR and SV in the tilted position**

Tilting caused an increase in HR and a decrease in SV compared with the values in the supine position (Table 1). The increase in HR is caused by reduced vagal activity in the tilted position (Saul et al. 1989), and the decrease in SV is caused mainly by reduced venous return. The reduction in SV may be partly counteracted by an increase in sympathetic-controlled contractility of the heart.

In the tilted control state, both RSA and variations in SV were smaller than in the supine control state. The smaller SV variation in the tilted position is probably due to the concomitant reduction in RSA, i.e. variation in cardiac filling time is reduced. In the tilted control state, there is smaller variability in CO than in the supine control state (n.s.), probably because both HR variability and SV variability are smaller, but HR variations still counteract SV variations in this position.

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**Figure 4. Phase angles between RE and the other variables in the supine and tilted positions**

The circles illustrate the respiratory cycle, and lines indicate the phase angle between RE and each variable. The dotted lines separate the four quadrants. A and B show the phase angles in the supine control state and after medication, respectively. C and D show the phase angles in the tilted control state and after medication, respectively. E shows how the recorded variables would appear if they were in exact phase or in exact inverse phase. Abbreviations as in Fig. 1.
In the tilted position, we found the same inverse relationship between HR and SV as in the supine control state and a decrease in variations in both HR and SV at respiratory frequency after atropine administration. CO variations increased after atropine administration due to the inverse relationship between HR and SV in the control states, as further explained below. Hence, RSA buffers CO variations in the tilted position as well as in the supine position.

Atropine administration induces a greater increase in CO variations in the tilted position than in the supine position because of the smaller reduction in SV variations. Saul et al. (1991) found that during propranolol and atropine administration, the purely mechanical effects were larger in the standing than in the supine position and that the magnitude of the mechanical effects increased with increasing breathing frequency. The changes in central venous pressure produced during respiration may have a greater impact in the tilted position than they have in the supine position.

**Synthesis of the findings on HR and SV in the supine and tilted positions**

Several factors contribute to the inverse relationship between HR and SV during the respiratory cycle. The mechanical reduction in SV during inspiration may be explained by increased capacity in the pulmonary vessels and ventricular interdependence (Jurgen et al. 1989). Inspiration causes a decrease in vagal nervous firing frequency at normal breathing frequencies, which increases HR, as reviewed by Saul & Cohen (1994). A higher HR reduces the filling time of the heart, and contributes to the decrease in SV. In addition, the mechanically induced fluctuations in SV will cause fluctuations in arterial blood pressure, which may reflexly change HR through baroreceptor impulses. These mechanisms cause a rise in HR and a decrease in SV during inspiration, and the opposite effect during expiration.

From the inverse relationship between SV and HR described above, it is clear that RSA elicits buffering of CO variations in the tilted position as well as in the supine position. However, the impact of respiration on SV differs between the two positions, SV changes at respiratory frequencies being more pronounced in the supine position (Fig. 3).

**Respiration-synchronous blood pressure fluctuations in the supine position**

In the supine position MAP variations increase after propranolol and atropine administration, whereas SP variations decrease. Hence, RSA buffers fluctuations in MAP, as shown by Toska & Eriksen (1993). However, RSA does not seem to buffer variations in SP, confirming the earlier results from Taylor & Eckberg (1996). The apparent contradiction between the two studies is thus resolved by the fact that the two groups analysed different aspects of arterial blood pressure. The different methods of abolishing HR variations in the two studies may therefore not be important.

**Blood pressure variations in the tilted position**

In the tilted control state, mean MAP and SP values are the same as in the supine control state. The absolute respiratory-synchronous fluctuations in MAP and SP are also equal in both control states (Fig. 3).

We found that fluctuations in both MAP and SP at respiratory frequency increased after vagal blockade with atropine in the tilted position. This confirms our hypothesis that RSA buffers respiration-synchronous fluctuations in MAP and SP in the tilted position (Toska & Eriksen, 1993; Taylor & Eckberg, 1996; Piepoli et al. 1997; Sloan et al. 1997). After atropine administration, MAP variability increases more than SP variability.

**Synthesis of the findings on MAP and SP in the supine and tilted positions**

Changes in arterial pressure may be caused by changes in CO, changes in TPR or changes in arterial compliance. In the time frame of respiratory variation, arterial pressure changes are caused solely by changes in CO, since changes in vascular resistance are too slow and there is no change in arterial compliance. MAP thus depends mainly on the combined effect of SV and HR on CO, and MAP variations therefore increase after medication when CO variations increase (Fig. 3B). On the other hand, SP depends on SV, ejection time, arterial stiffness and wave reflection.

In the tilted position, variations in MAP and CO increase in a parallel fashion, as they do in the supine position. However, in the tilted position, SP fluctuations increase while SV fluctuations decrease after cholinergic blockade. One explanation for the opposing effects on SP variations in the tilted and supine positions could be that the mechanical effect of respiration on SV is greater in the tilted position (Saul et al. 1991). A possible mechanism for this effect could be that tilting and the cholinergic blockade change the shape of the aortic systolic outflow pattern without changing the integrated stroke volume. This could cause greater variations in SP without changing the variations in SV significantly. Other possible explanations are a different afterload effect, higher contractility or changed compliance.

If we accept that MAP is buffered by RSA, we do not have to accept that two different mechanisms are operating in the tilted and supine positions, as has been proposed (Taylor & Eckberg, 1996; Cooke et al. 1999). It seems that RSA has greater physiological importance in the tilted position than in the supine position, since blood pressure variations are larger in the tilted position after RSA is eliminated (Fig. 3). We conclude that RSA plays an important role in buffering arterial pressure variations regardless of position.
Origin of RSA: central command or arterial baroreflexes?

The physiological relevance of RSA is still not clear (Toska & Eriksen, 1993; Saul & Cohen, 1994; Hayano et al. 1996; Piepoli et al. 1997). The physiological link between respiration and arterial pressure is dependent on various factors, which include species, posture, haemodynamic stress and respiratory frequency (Saul et al. 1991). RSA is probably a result of both feedback and feedforward mechanisms and hence causality cannot be inferred. Studies based on spectral analysis cannot distinguish between feedback (i.e. baroreflex) and feedforward mechanisms. Thus, the present study does not permit us to analyse the involvement of arterial baroreflexes in the generation of RSA. Nevertheless, previous studies using similar techniques have concluded that the arterial baroreflexes contribute insignificantly to the generation of RSA in the supine position (Taylor & Eckberg, 1996). On theoretical grounds, we believe that this conclusion is not valid, since cross-spectral analysis of the relationship between the arterial blood pressure and HR cannot be interpreted as characterizing either the feedforward from HR to arterial blood pressure or the baroreflex feedback from arterial blood pressure to HR (Saul et al. 1991). Consequently, the RSA expresses the combined effects of these mechanisms. In addition, Taylor & Eckberg’s conclusion is based on insufficient data, since MAP was not analysed. However, it is clear that neither arterial baroreceptors nor central command alone can fully explain RSA, nor can either of them be excluded as a contributing factor.

It seems rather unlikely that there is no baroreflex involvement in the generation of RSA. Respiratory variations in MAP are invariably expected to induce variations in HR caused by simple baroreflex mechanisms, since previous studies have shown that the baroreflexes express fluctuations in arterial pressure as HR variations at this frequency (Toska et al. 1994, 1996). A central command may be quantitatively more important in the generation of RSA. All the information we have used in this discussion is assembled in Fig. 5. As we see it, it is not possible to conclude whether the arterial baroreflexes are involved in the origin of RSA from the present experimental data. In order to reach a conclusion, a new and different experimental design must be introduced which includes a method for removing selectively the effect of the signals from the arterial baroreceptors.

Limitations of the study

Methodological differences between the studies we are comparing may have had an impact on their results. For example, various methods of eliminating respiration-synchronous HR variations have been used. Toska & Eriksen (1993) used atropine administration, while Taylor & Eckberg (1996) used oesophageal pacing. In our study we used atropine and propranolol. However, we were able to reproduce the findings of both the other studies.

Another difference between our study and that of Taylor & Eckberg was that we used spontaneous breathing, whereas Taylor & Eckberg used a fixed breathing frequency (0.25 Hz) (Taylor & Eckberg, 1996). This difference probably has no influence on the power spectra (Cooke et al. 1998).

Figure 4 illustrates fluctuations in the cardiovascular variables relative to respiration, but we wish to emphasize that this figure does not show whether the respiratory changes cause fluctuations in the cardiovascular variables or whether there is a central command that causes both respiratory and cardiovascular changes.

Figure 5. A simplified model of cardiovascular changes during normal inspiration

A simplified model of the cardiovascular changes during inspiration. The feedforward mechanism is illustrated as a direct connection between respiratory and cardiovascular control. The cardiovascular control increases HR during inspiration through the vagus nerve. The mechanical effects of inspiration increase the venous return to the right side of the heart, and then reduce SV from the left side of the heart due to ventricular interdependence, as explained elsewhere in the text. The higher HR then further decreases SV by reducing cardiac filling time. The higher HR also buffers CO, i.e. lessens the CO reduction produced by the lower SV. Reduction in CO causes a reduction in MAP, which elicits a baroreflex response to further raise the HR.
SV has a major impact on pulse pressure. We might be able to gain a better understanding of the relationship between arterial blood pressure and RSA by measuring pulse pressure instead of SP. However, SP, DP and pulse pressure are difficult to record non-invasively, whereas MAP may be recorded more reliably. The peripheral pressure waveform and thus SP and DP are distorted by pressure wave transmission and reflection in the peripheral arteries. These distortions will be cancelled out in the process of beat-synchronous averaging for MAP calculation. We also think that MAP is the more important variable to study. Previous studies have shown that when MAP and pulse pressure vary in opposite directions, MAP is the most important stimulus (Sanders & Ferguson, 1989).

Conclusions and implication of the study
RSA buffers respiration-synchronous fluctuations in MAP in both the supine and the tilted position. RSA plays an important role in buffering CO variations in both positions. The fluctuations in SP are buffered by RSA in the tilted position but not in the supine position.

Our study clearly shows that it is important to distinguish between the different aspects of arterial pressure when analysing fluctuations at respiratory frequency.

In further studies MAP must be included in the analysis, because, as our study shows, excluding this important input to the autonomic system from the analysis may lead to contradictory conclusions.