Snoring-related energy transmission to the carotid artery in rabbits

Jason Amatoury,1,2 Lauren Howitt,1 John R. Wheatley,1,3 Albert P. Avolio,2 and Terence C. Amis1,3

1Ludwig Engel Centre for Respiratory Research, Westmead Hospital, Sydney, New South Wales; 2Graduate School of Biomedical Engineering, University of New South Wales, Sydney, New South Wales; 3Faculty of Medicine, University of Sydney, Sydney, New South Wales, Australia

Submitted 15 November 2005; accepted in final form 25 January 2006

Snoring is a common consequence of an increase in upper airway resistance during sleep (1). Habitual snoring (every night or almost every night), without overt obstructive sleep apnea (OSA), is highly prevalent in the community, occurring in ~40% of men and 20% of women (2, 31, 46). Much attention has been focused on snoring as a social nuisance (13, 15), but over the last two decades there has been an increasing awareness of the possible health risks associated with habitual snoring. Epidemiological studies have identified snoring as a risk factor for a number of chronic cardiovascular diseases including hypertension (4, 24, 25, 45), myocardial infarction (7), ischemic heart disease (22), angina (21), and stroke (16, 28, 33, 34, 36, 41, 42).

Snoring sounds are generated in the upper airway during sleep and result from vibration of the pharyngeal wall and its associated structures (23). The carotid artery lies in close proximity to the pharyngeal wall, with the level of its bifurcation being adjacent to the hypopharynx. More than a decade ago, Hedner et al. (14) proposed that snoring vibrations, or more specifically oscillatory negative pressure waves originating in upper airway walls, may be transmitted through surrounding tissues to the carotid artery wall. They hypothesized that these vibrations, if repeated nightly over time, may result in two possible events: 1) initiation and promotion of carotid artery endothelial damage, a recognized pathogenic factor in the development of atherosclerosis; and/or 2) initiation and promotion of existing plaque rupture, leading to thrombus dislodgement and embolic stroke.

The juxtaposition of the hypopharynx and the carotid bifurcation, the major site of atherosclerotic lesions in the carotid artery (47), adds to the plausibility of this scenario. Under this paradigm, snoring vibrations can be viewed as a potential energy source for both the initiating (intimal injury) and terminating (plaque rupture) events of the “reaction to injury” cascade theory (39, 40) for the development of atherosclerosis. This hypothesis is further supported by the emergence of epidemiological data throughout the last decade that is increasingly suggestive of a linkage between snoring and cerebrovascular disease. To date, however, there have been no published studies that have attempted to test any aspect of this hypothesis. It is not known, for example, whether snoring-associated vibration energy is actually transmitted to the carotid artery walls, let alone whether snoring produces sufficient vibration energy to cause endothelial damage or initiate plaque rupture.

The aim of the present study was to use an animal model to quantify, for the first time, the energy levels present in the peripharyngeal tissues during snoring and to examine the extent of snoring vibration energy transmission across the carotid artery wall.

MATERIALS AND METHODS

Subjects

Studies were performed on six adult, male, New Zealand White rabbits [weight 3.1 ± 0.3 kg (mean ± SD)]. Protocols were approved by the Western Sydney Area Health Service Animal Ethics Committee.

Anesthesia

Anesthesia was induced with an intramuscular injection of ketamine (35 mg/kg) and xylazine (5 mg/kg) and then maintained with a continuous intravenous infusion of ketamine (15 mg·kg⁻¹·h⁻¹) and xylazine (4.5 mg·kg⁻¹·h⁻¹). Animals were euthanized at the completion of experiments.
pletion of each study by an overdose of intravenous sodium pentobarbital.

**Surgery**

All rabbits were studied in the supine position while breathing spontaneously and with the head and neck supported at 25° to the horizontal. A skin incision was made on the ventral surface of the neck, and the left (n = 4) or right (n = 2) common carotid artery was exposed via blunt dissection.

**Instrumentation**

Figure 1 illustrates the experimental setup. A transducer-tipped catheter (Millar SPR-524, Millar Instruments, Houston, TX) connected to a two-channel pressure control unit (Millar PCU-2000, Millar Instruments) was surgically inserted into the common carotid artery and advanced until its tip (with sensor orientated toward the upper airway) was estimated to be at the bifurcation into internal and external carotid arteries (i.e., approximately at the angle of the mandible). A ligature was placed around the common carotid artery to secure the catheter in place. This catheter was used to monitor carotid sinus luminal pressure (PCS).

A second catheter was surgically advanced through the tissues immediately adjacent to the common carotid artery wall to a position where its sensor, facing the upper airway, was at the same level as the tip of the intraluminal transducer. This latter catheter was used to monitor pressure in the tissues surrounding the carotid artery bifurcation (PCT). Correct positioning and orientation of both transducers were verified at postmortem examination. The pressure transducer catheters have a linear response between 0 and 10 kHz with an operating pressure range of −67.9 to +407.9 cmH2O.

Sound pressure (PSOUND) was measured by using a cardioid polar pattern studio condenser microphone (CAD M37, CAD Professional Microphones, Menton, OH) positioned at 30° to the vertical and at a distance of 2–2.5 cm from the rabbit’s mouth. The microphone has a frequency response of 20 Hz–20 kHz and operates linearly between 50 Hz and 3 kHz with a manufacturer-specified sensitivity of 15.9 mV = 1 Pa. The microphone was interfaced with a preamplifier (Symetrix SX202, Symetrix, Mountlake Terrace, WA), providing the signal with a gain of 55 dB.

**RESULTS**

**Time Domain**

Under TB conditions PCT was typically positive with fluctuations coinciding with respiration, i.e., 0.5–1 Hz (Fig. 3). For
the group, median baseline $P_{CT}$ was 1.5 (1.0–3.5) cmH$_2$O [median (interquartile range)].

Baseline $P_{CS}$ was characterized by cardiac cycle-related pressure oscillations (2–3 Hz) with a median pressure of 77.2 (33.5–87.2) cmH$_2$O for the group. Furthermore, $P_{CS}$ was also influenced by respiratory fluctuations. During TB $P_{SOUND}$ was reflective of room background.

When external neck compression was applied, median $P_{CT}$ increased to 6.2 (1.4–9.7) cmH$_2$O for the group and phasic high-frequency pressure oscillations that were not present during TB appeared on each of the pressure signals (Fig. 3). These oscillatory pressure bursts coincided with the auditory detection of snoring sounds. Respiratory-related lower frequency oscillations, present on the $P_{CT}$ and $P_{CS}$ signals during TB, increased in amplitude during IS. Median $P_{CS}$ during IS revealed no significant change from the TB value of 63.4 (33.7–78.4) cmH$_2$O.

**Frequency Domain**

When the data were examined in the frequency domain, snoring was associated with the development of power peaks at discrete frequencies above 50 Hz that were not present during TB (no new peaks below 50 Hz). Figure 4 shows representative examples of mean power spectra for $P_{SOUND}$, $P_{CT}$, and $P_{CS}$ ($P_{SOUND}$, $P_{CT}$, and $P_{CS}$, respectively) during TB and IS conditions.

Typically more than one power peak was detected during IS. For the $P_{SOUND}$ signal two snoring-associated power peaks were identified, one in the 100–400 Hz range (4 rabbits) and another between 250 and 700 Hz (all rabbits). For $P_{CT}$, peaks occurred at 60–170 Hz (all rabbits), 115–300 Hz (5 rabbits), 295–330 Hz (3 rabbits), and 440 Hz (1 rabbit). Power peaks detected on $P_{CS}$ were similar to those for $P_{CT}$.

**Energy**

In the 0–50 Hz bandwidth, there was a significant snoring-associated increase in energy for $P_{CT}$ during IS from 2.2 (1.1–12.3) cmH$_2$O$^2$ during TB to 39.0 (2.5–95.0) cmH$_2$O$^2$ ($P < 0.05$; Fig. 5A). The static (0 Hz) pressure component dominated this frequency range [its power accounting for 99.5 (96.8–99.5)% of the energy during TB and 97.5 (79.3–97.5)% during IS] increasing from 2.2 (1.1–12.3) cmH$_2$O$^2$ during TB to 38.1 (1.9–93.3) cmH$_2$O$^2$ during IS (borderline significant, $P = 0.075$). In contrast, although the static power associated with $P_{CS}$ tended to be greater than for $P_{CT}$, it was unaffected by IS (Fig. 5A), although the power dominance also apparent with its 99.9 (99.7–99.9)% contribution to the total energy during TB and IS. $P_{SOUND}$ in the 0–50 Hz region was not analyzed because of the microphone's inadequate frequency response in this region.

**50 Hz–1 kHz**

The upper limit of frequencies that contained 95% of the total energy present above 50 Hz (i.e., $F_{95}$) during IS was 652 (607–796) Hz for $P_{SOUND}$, 717 (583–708) Hz for $P_{CT}$, and 645 (564–709) Hz for $P_{CS}$. The energy contained in the 50-Hz to $F_{95}$ bandwidth increased significantly from TB to IS for $P_{SOUND}$ (6.0 (4.1–7.9) $\times 10^{-10}$ vs. 1.1 (0.8–1.7) $\times 10^{-8}$ cmH$_2$O$^2$), $P_{CT}$ (9.2 (8.3–10.4) $\times 10^{-4}$ vs. 172.0 (118.0–569.0) $\times 10^{-4}$ cmH$_2$O$^2$), and $P_{CS}$ (13.4 (8.5–18.0) $\times 10^{-4}$ vs. 151.0 (78.2–278.8) $\times 10^{-4}$ cmH$_2$O$^2$) (all $P < 0.03$). Figure 5B shows data for the energy associated with $P_{CT}$ and $P_{CS}$.

**Energy-Power Relationships for 95% BW**

When the energy ratios were examined for IS, only 5.9 (2.6–9.9) $\times 10^{-5}$% of the energy in the $P_{CT}$ signal and 7.8 (4.2–12.8) $\times 10^{-5}$% of the energy in the $P_{CS}$ signal were present in the $P_{SOUND}$ signal. However, when transmission across the carotid artery wall was examined, $P_{CS}$ energy was 90.5 (54.5–114.0)% of $P_{CT}$ energy.
Power transmission across the carotid artery wall during IS was examined for the group in relation to frequency (Fig. 6). In the 75–275 Hz frequency range, PCS power exceeded that for PCT (power ratio $/H_{11022}$ 1.0), whereas at frequencies above 275 Hz the power in the PCS signal was less than that in the PCT signal (power ratio $/H_{11021}$ 1.0). There was also greater power for PCS than PCT at frequencies between 0 and 75 Hz. This was true for both TB and IS states.

**DISCUSSION**

This study has established a new animal model in which snoring can be induced and quantified in terms of both sound production and the characteristics of the vibrations occurring in the peripharyngeal tissues. In particular, for the first time, this model allows snoring to be described in terms of the energy levels present within the tissue structures surrounding the upper airway. This approach was used to define the relationship between ambient sound pressure during snoring and associated vibration energy levels occurring both immediately adjacent to and within the carotid artery. In addition, quantitative relationships were established between snoring sound energy as measured by an ambient microphone and the vibration energy present both outside and within the carotid artery lumen. No previous study has directly measured the pressure oscillations that occur in upper airway wall tissues during snoring, let alone those occurring within the carotid artery lumen.

The main purpose of the present study was to examine the hypothesis that snoring-associated energy is transmitted to the carotid artery walls. The primary finding of this study was that snoring is associated with pressure vibrations both in the tissues surrounding the carotid artery wall and within the carotid sinus and that these vibrations are associated with frequency-dependent increases in carotid artery wall energy. These findings represent a first step in determining whether snoring vibrations contribute to the pathogenesis of carotid vascular disease. The significance and relevance of our data to cardiovascular disease lies in the establishment of a model in which snoring and carotid artery function can be studied and our use of this model to demonstrate snoring-related energy transmission to carotid artery walls.

**Critique of Methods**

Animal models for snoring have been reported previously using dogs (3), but this is the first description of a rabbit model...
for snoring. Although anesthetized rabbits have been used by a number of investigators to examine neuromechanical influences on upper airway function (19, 26, 32), there have been no previous analyses of snoring characteristics in rabbits. In the present study, the measured frequency content for rabbit snoring under the conditions of the present study revealed some differences from published reports for human snoring. Primarily, there was a tendency for rabbit snores to be characterized by higher primary frequencies than are typically reported for human snores. Reported dominant frequencies (i.e., frequencies with greatest power) for human snores fall between 30 and 150 Hz (3, 10, 27, 37). However, in the present study of rabbits, the dominant frequency ranged between 125 and 700 Hz. This probably reflects differences in upper airway anatomy, the mass of the oscillating tissues in rabbits vs. humans, and potential differences in the site of airway obstruction. However, similarities did exist between rabbit and human snores especially when focusing on patterns in the time and frequency domains. In this regard rabbit snores resembled the simple- and complex-waveform snores defined by Beck et al. (3) for humans. Also evident were changes between simple- and complex-waveform snores within a given snoring segment and even within a single snore; this has also been described in human studies (3, 37).

In our model, snoring is induced by applying a force to the skin surface of the neck. This has been shown to increase upper airway resistance in anesthetized rabbits (20), presumably by increasing the pressure in the tissues surrounding the pharyngeal airway (18). Anesthesia depresses upper airway dilator muscle activity (9, 29, 30), increasing the vulnerability of the upper airway to narrowing and collapse. In our model the compressive transmural pressure across the pharyngeal wall is increased to the point of wall instability and tissue vibration (i.e., snoring). Thus our findings relate to a model in which increased static pressure in the tissues is the initiating event for snoring. We have previously shown (18) that a number of mechanical influences can alter this tissue pressure and increase upper airway resistance (e.g., head/neck position, mandible position, and reduced tracheal traction forces).

Although the frequency content of snores obtained by using our model are, in general, similar to those reported for natural snoring in humans, small positioning and/or applied sandbag or digital pressure differences between studies may have contributed to some of the between subject variability that we observed in mean power spectra plots. However, innate biological properties may also cause variation within and between snoring segments (e.g., upper airway dilator muscle tone changes, tracheal traction effects associated with lung volume shifts). The precise site of airway narrowing achieved in our study is not known. Consequently, some of the between-animal variability in snore frequency content may also be attributable to differing sites of upper airway obstruction (27).

Snore sounds were detected by an ambient microphone specifically chosen to include a flat response in the primary frequency range of interest (50 Hz–1 kHz). The energy level for sounds recorded via a microphone is highly dependent on recording geometry. Consequently, the relationships established for tissue vs. ambient energy are specific to our study.

Tissue pressure oscillations during snoring were measured with pressure transducer-tipped catheters. Again site of measurement may well have influenced the energy detected. The positioning of these catheters was confirmed at postmortem examination for each study, but small variations in positioning may not have been detected. The positioning of a catheter within the lumen of the carotid artery and the interruption of blood flow associated with this procedure may have influenced the mechanical properties of the carotid artery wall (e.g., amount of wall distension, level of smooth muscle contraction) and, therefore, its vibration energy transmission properties.

Despite these limitations, our model appears useful for investigations that examine the fundamental physiological processes involved in snore production and the transmission of snoring-associated pressure vibrations through tissue structures in close proximity to the upper airway.

**Time Domain Observations**

Under TB conditions both \( P_{CT} \) and \( P_{CS} \) were greater than atmospheric pressure and demonstrated low-frequency oscillations (Fig. 3). For \( P_{CT} \), median values were similar to those we have recorded in the pharyngeal wall in previous studies (18) while the low-frequency oscillations were in phase with respiration (\(~1\) Hz). Respiratory fluctuations in upper airway extraluminal tissue pressures have been shown previously (18, 43, 44). Static pressures measured for \( P_{CS} \) reflected the occluded carotid artery preparation, and the low-frequency oscillations reflected transmitted pulse waves and relatively small respiratory fluctuations (Fig. 3).

With the application of the sandbag, static values for \( P_{CT} \) increased, while remaining approximately the same for \( P_{CS} \). High-frequency pressure vibrations were also detected by the ambient microphone with in-phase high-frequency oscillations appearing on the \( P_{CT} \) and \( P_{CS} \) signals. In addition, the respiratory-related phasic signals for \( P_{CT} \) and \( P_{CS} \) were amplified, probably reflecting increased pharyngeal luminal pressure fluctuations associated with increased upper airway resistance.

**Snoring Energy**

During snoring the energy present in the tissues and within the carotid artery lumen was greater than that retrieved at the microphone (\(~17,000\) times greater). This finding probably reflects the pressure losses that occur in the open system (room microphone) compared with the closed system formed by the tissues and carotid artery wall. Nevertheless, an important point emphasized by these findings is that energy levels detected by the most commonly used system for recording the sound energy associated with snores (room microphone) will be substantially less than the energy that actually exists in the tissues surrounding the upper airway. Because snoring is actually a tissue vibration phenomenon, ambient microphone measurements may reflect the level of ambient noise pollution but grossly underestimate the energy available to produce tissue damage within the snorer.

During snoring, energy in the 0–50 Hz frequency range increased \(~17\) fold in the tissues surrounding the carotid artery wall but did not change significantly within the carotid artery lumen (see Fig. 5A). The increase in energy in this frequency range was dominated by an increase in the static values (0 Hz), reflecting the increased tissue pressure associated with the application of the sandbag. This energy, however, was not transmitted to the carotid artery lumen, suggesting that the carotid artery wall provides a protective barrier to the trans-
mission of static tissue pressures of this magnitude. However, other frequencies in this bandwidth were transmitted into the carotid lumen (e.g., respiratory fluctuations at ~1 Hz; see Fig. 3) although their impact on the total energy in the 0–50 Hz bandwidth was insignificant because the 0-Hz component accounted for ~99.9% of the total energy.

For the frequency bandwidth containing 95% of the energy above 50 Hz, snoring was associated with a ~19-fold increase in energy in the tissues and ~11-fold within the carotid artery lumen (see Fig. 5B). This finding demonstrates, for the first time, that, as originally hypothesized by Hedner et al. (14), snoring is associated with an increase in energy levels within tissues and that this energy is transmitted to the carotid artery lumen.

Carotid Artery Wall Energy Transmission

The energy transfer function developed for each rabbit to describe the transmission of energy from the tissues to the carotid artery lumen during snoring was dominated by an amplification of lower end frequencies in the 95% BW, i.e., generally in the range of 75–275 Hz (see Fig. 6). Thus it appears that transmission of energy across the carotid artery wall is frequency dependent. A possible explanation for the amplification in energy in this frequency region is resonance of the arterial wall. The arterial wall is a nonhomogenous structure, constructed from numerous cells (e.g., muscle, endothelium, collagen, elastin, etc.) across its layers. A system or object that resonates does this at its natural frequency. Because the wall is made of many elements, each possessing its own natural frequency, there will be a range of frequencies at which the wall can resonate, thus explaining the broad amplification band seen in the transfer function of these rabbits. Low-frequency arterial wall resonance has been demonstrated previously in canine iliac (11, 12) and carotid arteries (17) and also human iliac arteries (11, 12, 35). It is thought that mechanical vibrations imposed on arterial walls cause alterations in wall elastin and vascular smooth muscle (8), thus leading to arterial dilatation (5).

The exposure of rat blood vessels to vibration at 60 Hz (consistent with a dominant frequency of human snoring) has been shown to cause vasoconstriction after only 5 min. In addition, injury of endothelial cells was noted after only 4 h of vibration, progressing to endothelial denudation at 9 days (4 h/day of exposure) (6). If arterial wall damage is possible because of imposed vibration, then snoring vibration damage to arterial walls has some plausibility as an atherogenic phenomenon. In support of this concept, one recently published study demonstrated that vibrating (at 60 Hz) human bronchial epithelial cell cultures initiated a proinflammatory response after only 12 h of exposure (38), another indication of the possibility of snoring vibration-induced endothelial injury.

In conclusion, to date there has been little attention paid to the implications of inducing oscillations in the tissues surrounding the upper airway beyond the generation of the annoying sound known as snoring. Although epidemiological evidence linking snoring with adverse health outcomes has grown over the years there has been little focus on the mechanisms that may be in play. The present study emphasizes that although snoring is usually assessed from the sound intensity detected by ambient microphones, far higher energy levels exist in the oscillating tissues themselves. The establishment of an animal model in which this phenomenon can be studied provides a mechanism for studying the health implications of snoring from a new perspective.

We conclude that during snoring, pressure vibrations occur in the tissues surrounding the carotid artery wall and are transmitted to the carotid artery lumen itself. Moreover, at least in rabbits, transmission of snoring vibrations across the carotid artery wall is associated with amplification in the 75–275 Hz range. Thus snoring vibrations present within the carotid artery wall may provide a potential energy source for carotid arterial wall damage and/or atherosclerotic plaque rupture.

ACKNOWLEDGMENTS

The authors thank Dr. Kristina Kairaitis for helpful discussion and manuscript preparation and the staff of the Ludwig Engel Centre for Respiratory Research for assistance.

GRANTS

This work was supported by the National Health and Medical Research Council and Department of Veteran’s Affairs, Australia. This study was supported by the National Health and Medical Research Council of Australia and the Department of Veteran’s Affairs.

REFERENCES


J Appl Physiol • VOL 100 • MAY 2006 • www.jap.org