Prevention or Attenuation of Baroreceptor Resetting by Pulsatility During Elevated Pressure

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SUMMARY Acute static elevation of arterial pressure increases the pressure threshold for activation of baroreceptors (acute resetting). The purpose of this study was to test the hypothesis that pulsatility during acute elevation of pressure modifies this acute resetting. Activity was recorded in 21 single baroreceptor units from the isolated carotid sinuses of dogs anesthetized with chloralose. Single-unit pressure thresholds were determined with a slow ramp increase in pressure. After a control period of static pressure at 25 to 50 mm Hg, the pressure threshold averaged 69 ± 4 (SE) mm Hg. Three graded levels of static pressure were held for 5 to 15 minutes. The levels averaged 76 ± 4, 115 ± 6, and 170 ± 6 mm Hg. The corresponding nerve activity during these periods was 0, 44 ± 6, and 63 ± 6 spikes per second, and the resulting increases in pressure threshold averaged 10 ± 1, 17 ± 2, and 26 ± 3 mm Hg, respectively. In contrast, during equivalent elevations of pulsatile pressure, nerve activity averaged 20 ± 3, 37 ± 4, and 61 ± 5 spikes per second, and the increases in pressure threshold averaged 0 ± 4, 14 ± 2, and 24 ± 2 mm Hg, respectively. In some units, the pressure threshold decreased following elevation of pulsatile pressure. The results indicate that: 1) pulsatility during elevation in pressure prevents or attenuates the acute baroreceptor resetting except at maximal pressure; 2) upward resetting occurs with elevation of static pressure even when there is no nerve activity during the period of elevated pressure; in contrast, with equivalent elevation of pulsatile pressure, resetting does not occur and occasionally the single-unit pressure threshold is reduced despite a significant increase in nerve activity during the period of pulsatile pressure. (Hypertension 9 [Suppl III]: III-137–III-141, 1987)

KEY WORDS • pulsatility • acute resetting • blood pressure regulation • mechanoreceptors • dogs

ELEVATION of static arterial pressure increases the pressure threshold ($P_o$) necessary to activate arterial baroreceptors. 1-3 This acute baroreceptor resetting occurs within 5 to 15 minutes after pressure elevation and is considered an important factor in the neural control of the circulation. 4-7 The mechanism of acute resetting is controversial. It has been suggested that mechanical changes in the properties of the vascular wall 8 and ionic alterations at the receptor level secondary to depolarization and subsequent activation of Na⁺,K⁺-adenosine triphosphatase (ATPase): 9 are involved.

We tested the hypothesis that pulsatility during elevated pressure may modify this acute baroreceptor resetting. Pulsatility may elicit myogenic vasoconstriction and enhance the myogenic response to an elevation of pressure. 10 The magnitude of change in vascular wall properties may therefore differ during pulsatile versus static pressure. In addition, the pattern and magnitude of baroreceptor activity is altered during pulsatile pressure and this may alter the ionic environment of the receptor. 11-14 Thus, pulsatility may modify the magnitude of resetting during elevations in pressure.

In this study, we contrasted the effect of increases in pressure from low static levels to graded levels of high static or high pulsatile pressure. We attempted to correlate the magnitude of baroreceptor resetting, measured as an increase in $P_o$, with the magnitude of nerve activity during the periods of elevated static or pulsatile pressure.
Methods

Mongrel dogs (16 to 24 kg) were anesthetized with thiopental sodium (30 mg/kg, i.v.) and α-chloralose (80 mg/kg, i.v.). Supplemental doses of α-chloralose were administered hourly. The dogs were intubated and mechanically ventilated with room air supplemented with oxygen. Arterial pH and partial pressure of carbon dioxide were maintained within normal limits by adjusting the ventilation and administering sodium bicarbonate when necessary. Catheteres were placed in a femoral artery and vein for pressure measurements and α-chloralose administration, respectively.

Isolated Carotid Sinus Preparation

The isolated carotid sinus and baroreceptor recording techniques have been described elsewhere and will be described here briefly. The left carotid sinus was surgically exposed, and all arteries in the vicinity of the sinus were ligated. Catheteres were placed in the common and external carotid arteries. The isolated sinus was flushed and filled with a physiological salt solution equilibrated with 95% O2-5% CO2 and warmed to 37°C. The sinuse was connected to a pressure reservoir and carotid sinus pressure (CSP) was measured through the external carotid catheter by a Statham transducer (Model P23AA, Statham, Hato Rey, Puerto Rico).

The mean level of CSP was controlled by adjusting a regulator valve connected to a pressurized air source. A voltage waveform generator fed sine wave pulses into an electromagnetical pressure converter (Millar, Houston, TX, USA) that was connected to the reservoir. Pulse rate and pulse pressure were set at 90 to 130 pulses/min and 30 to 40 mm Hg, respectively, and were maintained constant whenever pulsatile pressure was utilized. This pressure generating system made it possible to instantaneously convert static to pulsatile pressure and vice versa without changing the mean CSP.

Carotid Sinus Nerve Recordings

The carotid sinus nerve was cut near its junction with the glossopharyngeal nerve, placed on a dissection stage, covered with paraffin oil, and desheathed. The vago sympathetic trunk and other nerves innervating the sinus region were sectioned. Baroreceptor activity was recorded with a bipolar platinum electrode connected to a Grass high-impedance probe (Model HIP 511E, Grass, Quincy, MA, USA) and amplified by a Grass (P511) bandpass amplifier (high frequency cutoff 3000 to 10,000 Hz; low frequency cutoff 30 Hz). Nerve traffic was visualized on a dual-beam storage oscilloscope (Model 5113, Tektronix, Beaverton, OR, USA) and listened to through a loudspeaker. A nerve traffic analyzer that counts spikes exceeding a preselected voltage at 115 ±6 mm Hg, where activity was equal during static and pulsatile pressures.

Data Analysis

All data are expressed as the mean ± standard error of the mean (SEM). Paired t tests were used to test for significant differences, and p<0.05 was considered significant. When more than one comparison was made within a protocol, a Bonferroni adjustment of the significance level was made.

Results

Increases in static pressure from less than 50 mm Hg to levels of 76 ±4, 115 ±6, and 170 ±6 mm Hg increased Psa by 10 ±1, 17 ±2, and 26 ±3 mm Hg, respectively (Figures 1 and 2). In contrast, pulsatile pressure at equivalent mean pressures resulted in increases in Psa averaging 0 ±4, 14 ±2, and 24 ±2 mm Hg, respectively (see Figure 2). In four of nine receptors, there was a decrease in the Psa after the first level of elevated pulsatile pressure (see Figure 1, lower half). Thus, resetting was prevented by pulsatile pressure at 76 mm Hg and was attenuated at 115 mm Hg (see Figure 2).

Baroreceptor activity was absent during static pressure at 76 ±4 mm Hg but was increased (20 ±3 spikes/sec) during pulsatile pressure at the same level. Activity was greater during static than during pulsatile pressure at 115 ±6 mm Hg, and equal during
FIGURE 1. Nerve activity during a pressure ramp in a single carotid baroreceptor unit before and after two periods of elevated pressure, one static (upper half) and one pulsatile (lower half). Acute elevation of static pressure to a level insufficient to cause sustained activation of the unit caused an increase in pressure threshold ($P_a$) from 83 to 97 mm Hg. The diameter at threshold ($D_a$) was also increased by 10%. Conversely, acute elevation of pulsatile pressure to an equivalent level activated the unit, but the $P_a$ dropped to 71 mm Hg and $D_a$ was essentially back to the control level. Thus, pulsatile elevation in pressure not only prevented resetting but markedly decreased the $P_a$ and wall tension at threshold in this experiment.

Discussion

The results indicate the following. First, an acute increase in carotid sinus pressure from low levels of static pressure to three graded higher levels of static and pulsatile pressures at 170 ± 6 mm Hg (see Figure 2).

Five single units did not reset upward after elevation of static pressure from 28 ± 2 to 108 ± 7 mm Hg. In these units, exposure to high pulsatile pressure reduced $P_a$ significantly (Figure 3).

Second, the step increase in static pressure to 76 ± 4 mm Hg was not sufficient to cause sustained activity, yet it caused acute resetting. This has also been observed previously. Acute resetting has been attributed in part to an ionic mechanism. It has been proposed that the influx of Na into baroreceptor nerve terminals during elevated pressure causes depolarization of the generator potential, which in turn may activate Na$^+$,K$^+$-ATPase. The Na$^+$ pump-induced extrusion of Na$^+$ leads to hyperpolarization of the neuron and renders it less excitable. Indirect evidence support-
The physiological significance of this finding may relate to the buffering capacity of the arterial baroreceptor reflex. Acute upward resetting of baroreceptors during a rise in pressure reduces the buffering capacity of the reflex and offsets to some degree this compensatory mechanism. On the other hand, if acute resetting is minimized or reversed with pulsatile elevation in blood pressure, it would tend to preserve or enhance the buffering capacity of the reflex during sustained elevations of pressure.

Important questions still remain to be answered in this regard. Although we have shown that an increase from low static to elevated pulsatile pressure prevents or attenuates acute resetting, we do not know whether upward resetting occurs with an increase from low pulsatile to high pulsatile pressure in single units with constant frequency, pulse pressure, and rate of change of pressure. If this is true, the physiological significance of the phenomenon of acute resetting will require reevaluation.

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