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# Does the Aortic Smooth Muscle Wall Undergo Rhythmic Contractions During the Cardiac Cycle?

Mini-Review

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**Abstract**   Classically, the smooth muscle walls of the aorta and other large conduit arteries are believed to behave as passive elastic tubes undergoing periodic distension with the pulse wave. This is in contrast to data that suggest that an active contraction-relaxation cycle occurs in synchrony with the cardiac cycle. In this paper data are reviewed, and the conclusion is reached, that the aorta undergoes an active contraction in synchrony with the heartbeat. These contractions show an upstroke in tension during the rising phase of the pulse wave, prompting the nomenclature pulse synchronized contractions, or PSCs. PSCs are eliminated by blockers of neural transmission, and the pacemaker for these events resides in the right atrium, potentially allowing for coordination between cardiac and vascular contractility. Understanding the contractile behavior of the aortic smooth muscle wall may both yield new targets for therapeutics as well as help to further explain the etiology of cardiovascular disease processes.

**Key Words**   aorta, Windkessel model,  pulse synchronized contractions

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## 1. Introduction

Measurement of tension changes from the smooth muscle wall of the aorta and other large arteries *in vitro* generally show either quiescent baselines or rhythmic contractions that occur at a frequency much slower than the heart rate [1-3]. When there is a quiescent baseline, a slow tonic contraction occurs following addition of adrenergic agonists as well as other mediators [1]. When spontaneous rhythmic contractions occur, they are usually recorded at a frequency of 1 to 5 per minute, considerably slower than the cardiac cycle [2,3]. The lack of observing a fast rhythmicity in isolated aortic segments, as well as the slow rate of vascular smooth muscle contractions, have helped to lay the foundation for the Windkessel hypothesis [4,5]. With this hypothesis, the smooth muscle walls of the aorta and other large conduit arteries are considered to behave as passive elastic tubes without an active contraction occurring in synchrony with the heartbeat.

Several lines of evidence have been interpreted as consistent with the smooth muscle walls of large arteries behaving as passive elastic tubes. For example, Rushmer [6] measured pressure-

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circumference relationships in the dog aorta and observed that the pressure and circumference curves were not uniform during the different phases of the cardiac cycle. One explanation proposed was that energy was being imparted by the aorta to the blood (i.e., a contraction). However, the possibility of an active aortic contraction was discounted, as it was believed that the quantity of smooth muscle in the vessel was too small and responsiveness too slow to play a role in the cardiac cycle. Peterson et al. [7] studied mechanical properties of arteries in vivo. They analyzed simultaneous recordings of intra-arterial pressure and diameter in dogs. During their recording of 5,000 pulse waves they found no evidence for an active smooth muscle contraction in synchrony with the cardiac cycle.

In contrast to the above studies, several lines of evidence do support rhythmic smooth muscle activation occurring during the cardiac cycle and this evidence will be reviewed.

## 2. Evidence for Smooth Muscle Activation During the Cardiac Cycle

Heyman and colleagues [8-11] evaluated the relationship of the pulse wave and arterial wall contractions. They observed brachial artery mechanical activity in humans to be coupled to P-wave activity and suggested an active event in the smooth muscle vascular wall. Specifically, diameter changes occurred in advance of the pulse wave. Further studies done in human brachial artery and dog femoral artery were inconsistent with the vessels behaving as passive elastic tubes. Diameter changes were once again observed in advance of pulse pressure changes.

Mangel et al. [12-15] directly measured tension changes in dog and rabbit aortas and femoral and coronary arteries in vivo. Blood flow either was bypassed and tension recordings made in the bypassed segment or blood flow was clamped and tension recordings made distal to occlusion of blood flow. A 1:1 correlation was observed between pulse pressure changes and smooth muscle contractility [12, 13]. Initial experiments suggested the rhythmic tension changes were a relaxation [12]. With further investigation, it was clarified that an increase in tension was synchronous with the upstroke of the pulse wave, and these were denoted pulse synchronized contractions (PSCs) [13-16]. As shown in Figure 1, PSCs occur in a 1:1 frequency with pulsatile pressure changes.

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A major concern with identification of PSCs is whether they could represent an artifact related to movement of heart. Several lines of evidence have been pursued to confirm that PSCs do not result from a cardiac movement artifact: (i) local application of the neural transmission blockers tetrodotoxin (TTX) or Xylocaine [12, 16] blocked PSCs without affecting the pulse wave or cardiac contractility; (ii) following bleeding of animals, in which there was no pulsatile pressure changes, PSCs were observed to persist [13], and under these circumstances, PSCs could not represent a movement artifact related to the pulse wave; (iii) excision of the right atrial appendage, but not left, resulted in abolition of PSCs even though cardiac contractions persisted [13]. These experiments led to the conclusion that the pacemaker region for PSCs resides in the right atrium, similar to the heart, and a dissociation of PSCs from cardiac contractility was further established.

Stimulation of the right atrial region was found to drive the frequency of PSCs [13]. PSCs were locked in frequency to the right atrial stimulation rate even when animals went into heart block and the ventricular rate was substantially slower than the atrial stimulation rate [13]. Shown in Figure 2 is an example of this phenomenon. PSC frequency was entrained to the right atrial stimulation rate while large, slow ventricular muscle contractions were seen, and these did not distort PSCs [13]. This study type also strongly supports PSCs not resulting from a ventricular muscle movement artifact.

Further evidence for the pacemaker for PSCs residing in the right atrial region was provided by Ravi and Fahim [16], who stimulated the sinoatrial nodal region in cat pulmonary arteries. When stimuli were applied during times when the heart was mechanically quiescent, an ectopic PSC was produced; during this time, no corresponding pulse wave was induced. These experiments further confirm a dissociation between cardiac contractility and PSC generation, as well as implicate the right atrial region as the pacemaker site for PSCs.
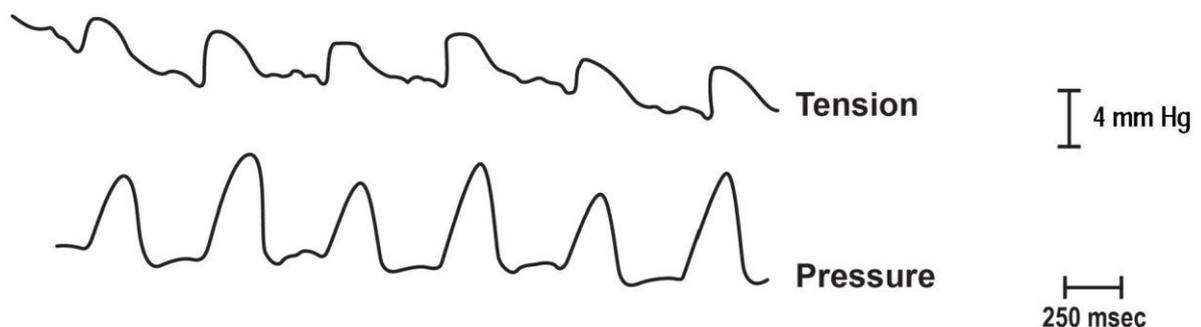
### 3. Discussion

Data are reviewed that challenge the century-old Windkessel-type description of aortic smooth muscle contractile behavior. The contractions are phased such that an increase in tension and upstroke of the pulse wave are synchronized, suggesting the nomenclature of pulse

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synchronized contractions, or PSCs. These events are neurogenically mediated, as evidenced by their sensitivity to TTX and Xylocaine. Although the specific role for PSCs has not yet been elucidated, their phasing suggests that PSCs may reduce distension of the wall by the pulse wave, thus reducing the Laplacian forces acting on the vessel wall [13].
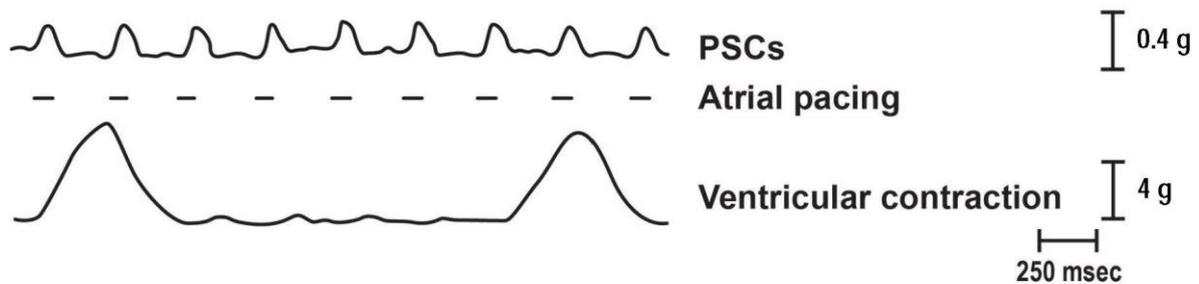
The following conclusions may be made:

i. The classical view of the smooth muscle walls of large conduit arteries, including the aorta, is that they behave as passive elastic tubes.

ii. Data have accumulated that the aortic smooth muscle wall undergoes a contraction relaxation cycle in synchrony with the cardiac cycle.

iii. The phasing of the contractions is such that the upstroke of the contraction wave occurs during increases in pulsatile pressure, yielding the term pulse synchronized contractions, or PSCs.

iv. PSCs appear to originate from a pacemaker in the right atrium, possibly to ensure coordination between cardiac and vascular contractility.

v. PSCs are of neurogenic origin and as such are TTX sensitive.

vi. Recognition and understanding of PSCs may both yield an additional target for therapeutics in the treatment of cardiovascular diseases as well as help to understand the etiology of these disorders.

## 4. Figures



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**Figure 1.** Simultaneous recording of wall tension and pulse pressure changes from rabbit aorta *in vivo*. Tension was measured with a balloon-tipped catheter [13] from a bypassed aortic segment. As noted, a 1:1 correspondence between tension and pulse pressure changes were observed. Modified from reference 13 with permission. (Cal Bar for lower trace 33 mmHg)



**Figure 2.** Recording of aortic PSCs and ventricular muscle contractions in a bled rabbit. Right atrial pacing frequency is indicated by the dashed line. Heart block occurred during right atrial pacing such that ventricular muscle contraction frequency was significantly slower than the atrial stimulation rate. Aortic PSCs were measured with a balloon-tipped catheter system and ventricular muscle contractions with a tension transducer. From reference 13 with permission.

## 5. Acknowledgments

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