ECRONICON OPEN ACCESS

EC CARDIOLOGY
Mini Review

Pulse Synchronized Contractions (PSCs): An Invited Review

Tobin P Mangel[1], Katherine Lothman[2] and Allen W Mangel[2]*

[1]*Adult Critical Care Unit, St. George's Hospital, London. UK*

[2]*RTI Health Solutions and Discovery Sciences, Research Triangle Park, NC, USA*

***Corresponding Author:** Allen Mangel, RTI Health Solutions and Discovery Sciences, Research Triangle Park, NC, USA.

Received: February 12, 2021; **Published:** March 19, 2021

Abstract

Cardiovascular diseases represent a significant factor contributing to morbidity and mortality in humans. Marked advancements have occurred in the development of novel therapeutics and procedures intended to improve cardiovascular functioning and reduce mortality rates. One area that continues to have limited diagnostic attention and, therefore, therapeutics is the spontaneous rhythmic contractions of the arterial walls that occur in synchrony with the heartbeat. Pulse synchronized contractions may represent an untapped opportunity for improvement in treatment of cardiovascular disorders. This paper reviews the essence of the literature on pulse synchronized contractions.

Keywords: *Cardiovascular System; Vascular Smooth Muscle; Pulse Synchronized Contractions; Neurogenic; Pacemaker*

Abbreviations

PSCs: Pulse Synchronized Contractions; TTX: Tetrodotoxin

Introduction

Heyman and colleagues [1-3], in a series of studies conducted between 1957 - 1961, evaluated in human brachial arteries and canine femoral arteries the relationship between pulse waves and changes in arterial diameter. It was noted that extra-arterially recorded brachial pulses can precede intra-arterially recorded pulse waves. Thus, this was interpreted to indicate that changes in arterial diameter preceded distension of the vessels from the pulse wave. The significance of these findings is that a contraction occurs in the smooth muscle wall of the vessel in advance of the pulse wave.

The temporal difference between the two events (i.e. pulse wave and diameter change) was determined to have a neurogenic basis, as it was eliminated by stellate ganglion block [3]. Heyman and colleagues concluded, based on these studies, that the smooth muscle wall of large conduit arteries does not behave according to the classical Windkessel description by Frank [4] but, rather, the vessel wall demonstrates active contractions in synchrony with the heartbeat.

Although the observations of Heyman and others have been previously reviewed, they remain principally ignored. Development of therapeutics to either modulate or correct malfunction of rhythmic arterial contractility or pulse synchronized contractions (PSCs) may represent a marked advancement in cardiology. Herein, we review the foundation for identification of PSCs. As discussed in the Conclusion, we have previously reviewed extensively the information on PSCs. However, in this invited review, we re-review this information because of the importance of this topic.

PSCs: Why were they potentially evaluated?

The smooth muscle wall lining the viscera of the gastrointestinal tract generates rhythmic contractile activity often triggered by spontaneous electrical events denoted slow waves and spikes [5]. Many studies conducted *in vitro* with muscle strips in organ baths showed no contractions elicited by depolarization during incubation in calcium-free solution containing a calcium chelator. However, we showed that with larger muscle segments, still evaluated *in vitro*, contractions occurred spontaneously or following electrical stimulation in these calcium-free solutions [6-8]. Thus, it was disproven that, for gastrointestinal smooth muscle, "trigger calcium" was required to observe depolarization-mediated contractions in the absence of extracellular calcium.

Based on the above observations, we studied whether a similar phenomenon occurs with vascular smooth muscle. Segments of aortic smooth muscle, whether large segments or small strips, show no spontaneous activity *in vitro* [9]. When studied in the absence of extracellular calcium (no added calcium plus a calcium chelator), no contractile activity was observed. However, fast rhythmic electrical events were observed [9] (Figure 1). These studies demonstrated that the aortic smooth muscle wall has the ability to generate fast rhythmic electrical activity. We hypothesized, based on these results, that the smooth muscle wall of large arteries may, therefore, possess the ability to generate rhythmic contractile activity *in vivo*.

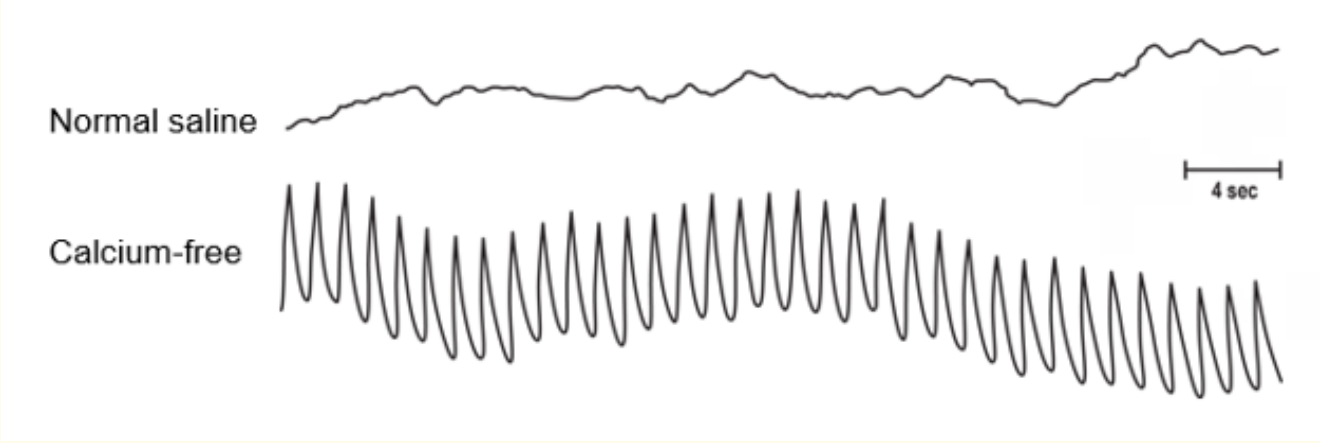

Figure 1: *Incubation of aortic segments from rabbits in normal saline are electrically quiescent (upper trace). In calcium-free solution containing a calcium chelator, a fast rhythmic electrical event is produced (lower trace) [9].*

Identification of PSCs

We bypassed blood flow from *in vivo* segments of rabbit aorta and dog carotid and femoral arteries [10-14]. Animals were instrumented such that contractions were recorded in the bypassed segments and pulse pressure measured intraarterially in a region very close to the bypassed segment. As shown in figure 2, contractions were noted in the bypassed segment, with the phasing demonstrating the upstroke of the contraction wave precedes the upstroke of the pulse wave [11-14]. Considering the temporal relationship between the two events, it was concluded that distension from the pulse wave did not produce the contractile event or PSC. However, as pulse waves could clearly not be measured in bypassed segments, it can be argued that the phasing is a reflection of differential recording locales. However, as PSCs were recorded in bypassed segments, they are not resultant from mechanical distension of the vessel by the pulse wave. Furthermore, PSCs could be recorded in bled animals [11].

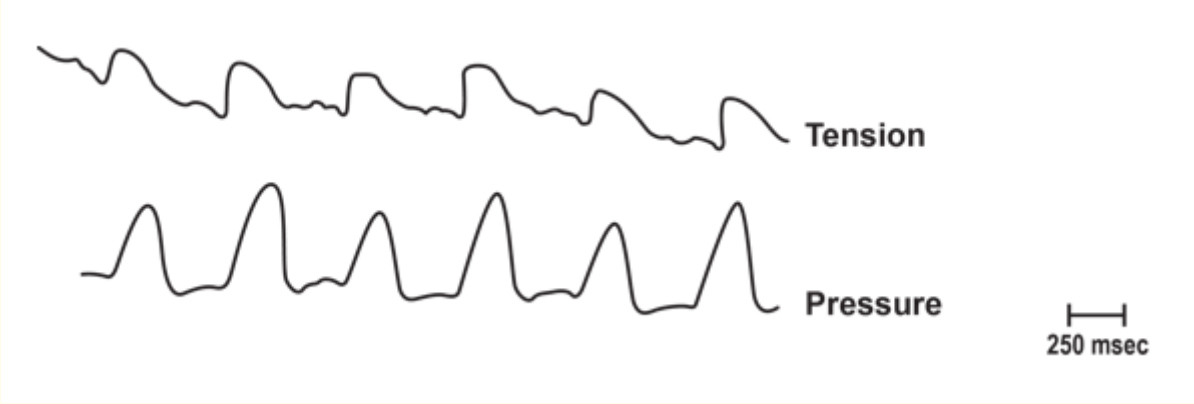

Figure 2: *Rhythmic tension changes (pulse synchronized contractions [PSCs]) were recorded with a 1:1 correspondence to the pulse wave from this anesthetized rabbit [11].*

As PSCs are not observed *in vitro*, it is possible that *in vivo* PSCs are secondary to neurogenic activation. To test this postulate, the neurotoxin tetrodotoxin (TTX) was applied to *in vivo* bypassed segments displaying PSCs, and PSCs were blocked [10,12,13]. We observed no change in cardiac contractility or the pulse wave with local application of TTX to the bypassed segment. Other neural blockers also reduced or abolished PSCs.

Considering the above, we next studied whether the pacemaker for PSCs may reside in the heart, as the pulse wave and PSCs were locked in frequency and phasic relationship. Excision of the right but not left atrial region in bled animals caused elimination of PSC activity [11]. This occurred even after the heart was electrically stimulated to levels greater than prior to atrial excision. Pacing of the heart to supra-baseline levels, prior to right atrial excision in bled animals, resulted in PSCs of enhanced frequency tracking the frequency of right-atrial stimulation [11]. All of these observations support the pacemaker region for the PSC residing in the right atrium.

Conclusion

Considering the significant morbidity and mortality associated with cardiovascular diseases, understanding the pathophysiologic role of PSCs is paramount. These neurally-activated contractions in animals and man simply demand much greater characterization *in vivo*. PSCs in animal models can be modulated by agents interacting with the sympathetic or parasympathetic nervous systems [10-13]. Therefore, the study of PSCs in humans under *in vivo* conditions, requires evaluation to determine whether these agents are altering PSC activity. It has been suggested that PSCs serve a protective function for the arterial wall, based on the phase relationship between the PSC and pulse wave [11-13]. PSCs may limit the distension of the vessel wall from the pulse wave thus, decreasing the Laplacian Forces acting on the wall. Reduction in these shearing forces may help to prevent aneurysm and dissection from occurring [11-13].

The pacemaker for PSCs residing in the right atrial region represents another example of the excellent synchrony and coordination of the cardiovascular system. We have recently reviewed PSCs [14-19], but, as discussed earlier, due to the significance of this topic, we re-review this information and the foundation for PSCs in this invited review.

Bibliography

1. Heyman F. "Comparison of intra-arterially and extra-arterially recorded pulse waves in man and dog". *Acta Medica Scandinavia* 157 (1957): 503-510.

2. Heyman F. "The arterial pulse as recorded longitudinally, radially and intra-arterially on the femoral artery of dogs". *Acta Medica Scandinavia* 170 (1961): 77-81.

3. Heyman F and Stenberg K. "The effect of stellate ganglion block on the relationship between extra- and intra-arterially recorded brachial pulse waves in man". *Acta Medica Scandinavica* 171 (1962): 9-11.

4. Frank O. "Die Grundform des Arteriellen Pulses". *Zeitschrift fur Biologie* 37 (1899): 483-526.

5. Prosser CL and Mangel AW. "Mechanisms of spike and slow wave pacemaker activity in smooth muscle cells". In: Cellular Pacemakers, Volume 1., ed. D. Carpenter. New York: John Wiley and Sons (1982): 273-301.

6. Mangel AW., *et al.* "Contractions of cat Small intestinal smooth muscle in calcium-free solution". *Nature* 281 (1979): 582-583.

7. Mangel AW., *et al.* "Depolarization-induced contractile activity of smooth muscle in calcium-free solution". *American Journal of Physiology* 242.11 (1982): C36-40.

8. Marion SB and Mangel AW. "From depolarization-dependent contractions in gastrointestinal smooth muscle to aortic pulse-synchronized contractions". *Clinical and Experimental Cardiology* 7 (2014): 61-66.

9. Mangel A and van Breemen C. "Rhythmic electrical activity in rabbit aorta induced by EGTA". *The Journal of Experimental Biology* 90 (1981): 339-342.

10. Mangel A., *et al.* "Rhythmic contractile activity of the in vivo rabbit aorta". *Nature* 289 (1981): 692-694.

11. Mangel A., *et al.* "Control of vascular contractility by the cardiac pacemaker". *Science* 215 (1982): 1627-1629.

12. Mangel A., *et al.* "Measurement of the in vivo mechanical activity and extracellular Ca-45 exchange in arterial smooth muscle". In: Vascular Neuroeffector Mechanisms: 4th International Symposium., ed. J. Bevan et al. Raven Press (1983): pp. 347-351.

13. Sahibzada N., *et al.* "Rhythmic aortic contractions induced by electrical stimulation in vivo in the rat". *PLOS One* 10.7 (2015): 1-10.

14. Mangel AW. "Does the aortic smooth muscle wall undergo rhythmic contractions during the cardiac cycle?" *Experimental and Clinical Cardiology* 20 (2014): 6844-6851.

15. Mangel AW. "A changing paradigm for understanding the behavior of the cardiovascular system". *Journal of Clinical and Experimental Cardiology* 8 (2017): 496.

16. Mangel A and Lothman K. "Emergence of a new paradigm in understanding the cardiovascular system: pulse synchronized contractions". *Cardiovascular Pharmacology* 6 (2017): 220.

17. Mangel AW and Lothman K. "Pulse synchronized contractions (PSCs): a call to action". *Open Journal Cardiology and Heart Disease* 1 (2018): OJCHD.000508.

18. Mangel A and Lothman K. "Emergence of a new paradigm in understanding the cardiovascular system: pulse synchronized contractions." (Reprinted) Top 10 Contributions on Cardiology". *Avid Sciences Publishers* (2018): 2-10.

19. Mangel AW., *et al.* "Pulse synchronized contractions: a review". *EC Cardiology* 7(2020): 61-66.

Volume 8 Issue 4 April 2021