Letters to the Editor will be published, if suitable, as space permits. They should not exceed 1000 words (typed double-spaced) in length and may be subject to editing or abridgment.

Letter by Villa Abrille et al Regarding Article, "Hyperactive Adverse Mechanical Stress Responses in Dystrophic Heart Are Coupled to Transient Receptor Potential Canonical 6 and Blocked by cGMP-Protein Kinase G Modulation"

To the Editor:

The recent article by Seo et al,[1] published in *Circulation Research*, presented many interesting aspects of the myocardium from mice lacking transient receptor potential canonical channels TRPC3 or TRPC6, from dystrophic animals, and their interaction with cGMP. These authors measured the muscle response to stretch, widely known as slow force response (SFR).

We would like to comment only on one aspect of this study that, although it might sound trivial at first glance, it unnecessarily confuses a well-established mechanical response. The authors arbitrarily changed the widely accepted denomination of SFR[2–14] by the term **s**tress-stimulated contractility without any explanation to justify the change.

The SFR or Anrep effect was described by Glen von Anrep in 1912[15] in a whole heart preparation and later on found in isolated cardiac preparations by Parmley and Chuck,[16] Lakatta and Jewell,[17] who called this mechanism slow increase in develop tension, and a few years later (1982) by Allen and Kurihara[18] who in addition demonstrated that this slow phase of tension increase after a change in length was because a progressive increase in the calcium transient. The scientific community has accepted the term SFR to identify this powerful intrinsic heart mechanism to adapt cardiac output to changes in hemodynamic conditions, mechanism that is being exhaustively analyzed because of the similarity of its intracellular signaling pathway to that leading to myocardial hypertrophy.[19]

We are sure that the authors from this prestigious University where we all 3 spend unforgettable times doing research can be more creative than changing the name to the SFR.

Disclosures

None.

María Celeste Villa-Abrille
Néstor Gustavo Pérez
Horacio Eugenio Cingolani
Centro de Investigaciones Cardiovasculares
Facultad de Ciencias Médicas de La Plata
UNLP-CONICET, Argentina

References

1. Seo K, Rainer PP, Lee DI, Hao S, Bedja D, Birnbaumer L, Cingolani OH, Kass DA. Hyperactive adverse mechanical stress responses in dystrophic heart are coupled to transient receptor potential canonical 6 and blocked by cGMP-protein kinase G modulation. *Circ Res*. 2014;114:823–832. doi: 10.1161/CIRCRESAHA.114.302614.
2. Alvarez BV, Perez NG, Ennis IL, Camilion de Hurtado MC, Cingolani HE. Mechanisms underlying the increase in force and Ca(2+) transient that follow stretch of cardiac muscle: a possible explanation of the Anrep effect. *Circ Res*. 1999;85:716–722.
3. Kockskämper J, Khafaga M, Grimm M, Elgner A, Walther S, Kockskämper A, von Lewinski D, Post H, Grossmann M, Dörge H, Gottlieb PA, Sachs F, Eschenhagen T, Schöndube FA, Pieske B. Angiotensin II and myosin light-chain phosphorylation contribute to the stretch-induced slow force response in human atrial myocardium. *Cardiovasc Res*. 2008;79:642–651. doi: 10.1093/cvr/cvn126.
4. Kockskämper J, von Lewinski D, Khafaga M, Elgner A, Grimm M, Eschenhagen T, Gottlieb PA, Sachs F, Pieske B. The slow force response to stretch in atrial and ventricular myocardium from human heart: functional relevance and subcellular mechanisms. *Prog Biophys Mol Biol*. 2008;97:250–267. doi: 10.1016/j.pbiomolbio.2008.02.026.
5. von Lewinski D, Kockskämper J, Zhu D, Post H, Elgner A, Pieske B. Reduced stretch-induced force response in failing human myocardium caused by impaired Na(+)-contraction coupling. *Circ Heart Fail*. 2009;2:47–55. doi: 10.1161/CIRCHEARTFAILURE.108.794065.
6. von Lewinski D, Stumme B, Fialka F, Luers C, Pieske B. Functional relevance of the stretch-dependent slow force response in failing human myocardium. *Circ Res*. 2004;94:1392–1398. doi: 10.1161/01.RES.0000129181.48395.ff.
7. von Lewinski D, Stumme B, Maier LS, Luers C, Bers DM, Pieske B. Stretch-dependent slow force response in isolated rabbit myocardium is Na+ dependent. *Cardiovasc Res*. 2003;57:1052–1061.
8. Kockskamper A, von Lewinski D, Zhu D, Kockskamper J, Khafaga M, Schmidt AG, Post H, Pieske B. Relevance of stretch-induced phosphorylation of MAPK and p90rsk in human myocardium. *Front Biosci (Elite Ed)*. 2013;5:883–892.
9. Calaghan S, White E. Activation of Na+-H+ exchange and stretch-activated channels underlies the slow inotropic response to stretch in myocytes and muscle from the rat heart. *J Physiol*. 2004;559:205–214. doi: 10.1113/jphysiol.2004.069021.
10. Niederer SA, Smith NP. A mathematical model of the slow force response to stretch in rat ventricular myocytes. *Biophys J*. 2007;92:4030–4044. doi: 10.1529/biophysj.106.095463.
11. Ward ML, Williams IA, Chu Y, Cooper PJ, Ju YK, Allen DG. Stretch-activated channels in the heart: contributions to length-dependence and to cardiomyopathy. *Prog Biophys Mol Biol*. 2008;97:232–249. doi: 10.1016/j.pbiomolbio.2008.02.009.
12. Shen X, Cannell MB, Ward ML. Effect of SR load and pH regulatory mechanisms on stretch-dependent Ca(2+) entry during the slow force response. *J Mol Cell Cardiol*. 2013;63:37–46. doi: 10.1016/j.yjmcc.2013.07.008.
13. Monasky MM, Biesiadecki BJ, Janssen PM. Increased phosphorylation of tropomyosin, troponin I, and myosin light chain-2 after stretch in rabbit ventricular myocardium under physiological conditions. *J Mol Cell Cardiol*. 2010;48:1023–1028. doi: 10.1016/j.yjmcc.2010.03.004.
14. Castro-Ferreira R, Neves JS, Ladeiras-Lopes R, Leite-Moreira AM, Neiva-Sousa M, Almeida-Coelho J, Ferreira-Martins J, F Leite-Moreira A. Revisiting the slow force response: the role of the PKG signaling pathway in the normal and the ischemic heart. *Rev Port Cardiol*. 2014;33:493–499. doi: 10.1016/j.repc.2014.03.006.
15. von Anrep G. On the part played by the suprarenals in the normal vascular reactions of the body. *J Physiol*. 1912;45:307–317.
16. Parmley WW, Chuck L. Length-dependent changes in myocardial contractile state. *Am J Physiol*. 1973;224:1195–1199.
17. Lakatta EG, Jewell BR. Length-dependent activation: its effect on the length-tension relation in cat ventricular muscle. *Circ Res*. 1977;40:251–257.
18. Allen DG, Kurihara S. The effects of muscle length on intracellular calcium transients in mammalian cardiac muscle. *J Physiol*. 1982;327:79–94.
19. Cingolani HE, Pérez NG, Cingolani OH, Ennis IL. The Anrep effect: 100 years later. *Am J Physiol Heart Circ Physiol*. 2013;304:H175–H182. doi: 10.1152/ajpheart.00508.2012.

(*Circ Res*. 2015;116:e11. DOI: 10.1161/CIRCRESAHA.114.305543.)

Circulation Research
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Letter by Villa Abrille et al Regarding Article, "Hyperactive Adverse Mechanical Stress Responses in Dystrophic Heart Are Coupled to Transient Receptor Potential Canonical 6 and Blocked by cGMP-Protein Kinase G Modulation"

María Celeste Villa-Abrille, Néstor Gustavo Pérez and Horacio Eugenio Cingolani

Circ Res. 2015;116:e11
doi: 10.1161/CIRCRESAHA.114.305543
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7330. Online ISSN: 1524-4571