Response to Letter from Villa-Abrille et al

As Drs. Villa-Abrille, Perez, and Cingolani correctly point out, the behavior whereby cardiac muscle is subjected to abruptly increased systolic load and then manifests a gradual rise in contractility has been recognized for over a century. First credited to Gleb (not Glen) von Anrep, its name has morphed over the decades along with the types of experiments used to generate it. The name, slow force response (SFR), has indeed been adapted by many to describe this behavior, but we feel the term is far less universal than the writers suggest, and also believe it obfuscates the mechanistic concepts behind it. What is slow—force or response? What is the response to and what does it reflect? Part of the reason we came up with our name is we wanted to target a broad readership who might not be as familiar with SFR—but would more immediately understand the concept of a stress-mediated rise in contractility, which is what is ultimately going on.

A simple PubMed search of the term slow force response yields 42 references, nearly half of which are from the letter writers themselves, and so we can understand their fondness for it. Nearly all these studies were performed in isolated muscle or myocytes—the majority using isometric contractions. When one adds the keyword in vivo to the search, no references return. Searching Anrep yields nearly 80 references, yet 90% of them do not mention SFR, so this is not a sine qua non terminology. In vivo, manifestations of the behavior have been called homeometric autoregulation, a term coined by Stanley Sarnoff in his 1960 description of a ventricle’s ability to augment cardiac output, despite a rise in systolic afterload and at a similar filling pressures. Other terms recognized by the behavior’s underlying dependence on contractility, such as slow inotropic response or inotropic response to mechanical stretch. Still another group of studies describes how altering load affects action potential duration and arrhythmia—behavior termed contraction-exitation or mechano-electric coupling, and often associated with stretch-activated channels.

In our study, isolated loaded myocytes contracted and shortened simultaneously, and what was mechanically altered was net autonomic stress, not only length. The response was related to a rise in calcium-coupled contractility and arrhythmia. This behavior was revealed in cells, but also in the intact heart where force was not the indexing parameter but rather a surrogate for contractility was. We settled on the term stress-stimulated contractility as we thought it conveyed what was happening more explicitly than SFR and would be more easily understood by a broader muscular dystrophy/heart failure readership. We also felt the term better captures the behavior both in vitro and in vivo. Although arguably creative, it was not meant to confuse. Rather, to paraphrase Shakespeare, (and you knew this was coming) “What’s in a name? That which we call SFR by any other name would still be due to stress-stimulated contractility.”

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None.


References
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