CONCERNING THE VALIDITY OF GASTROINTESTINAL EXTRACELLULAR RECORDINGS

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TO THE EDITOR: In their recent review “Interstitial cells: regulators of smooth muscle function,” Sanders, Ward, and Ko offer a comprehensive perspective on the features and functions of interstitial cells (11). However, several of the authors’ claims in their discussion of gastrointestinal extracellular recordings (Section II.E.1) require rebuttal, notably their statement that “extracellular electrical recording from visceral smooth muscle may be largely artifacts of contractile movement.” They further claim that “it is reasonable to be skeptical about the results of classic studies that have based major conclusions upon this technique.” A later paragraph lists unreferenced reasons why recording “authentic electrical activity in GI muscles with extracellular electrodes” cannot be achieved.

These criticisms have now been thoroughly discredited (1, 7, 9, 10, 12). The claims were based on a single murine study (2), performed in vitro, a context in which extracellular recordings are challenging and may be unreliable due to the effects of tissue isolation (7, 9, 12, 13). Indeed, no potentials were ever recorded in this study that could be regarded as representative of slow waves (7). This was likely because extracellular methods were incorrectly applied (7), including the use of filters that excluded the dominant frequency range in which slow waves occur (10).

We recently presented a comprehensive validation of extracellular slow wave recordings in the Journal of Physiology (1). In vivo extracellular recordings were performed in pig intestine, with contractile motion simultaneously inhibited by intraarterial nifedipine administration, clearly demonstrating slow wave recordings in the absence of contractions. A direct comparison of extracellular recordings from suction and conventional metal electrodes was also performed, showing conclusive consistency with respect to intracellular slow wave morphologies, activation-recovery intervals, and biophysically based modeling. Together, these findings represent convincing evidence for the validity of extracellular techniques, when correctly performed (1).

While Sanders et al. discussed our validation study in their review, we are concerned that they misrepresented our work (11). They claim our study “falls well short of a suitable control study for extracellular recording” because it “relied only on visual inspection” to verify that movement was blocked, and that “more rigorous monitoring of movement than visual inspection would be needed to detect the small movements capable of eliciting electrical artifacts.” In fact, our study did not rely on visual inspection. We applied rigorous computational methods of high-definition video analysis, generating strain maps to single-pixel (sub-millimeter) resolution (1). They also state that “no concentration/effect data for dihydropyridines were provided” and that “dihydropyridines don’t block all contractile movements in many species.” These claims also fail to fairly reflect our study, because concentration data for nifedipine were provided, and contractions were effectively blocked at these doses in the video analyses.

Readers of Physiological Reviews should be reassured that the vast and important literature based on extracellular methods remains valid. Indeed, within the field of interstitial cells, extracellular techniques play an especially important role because they are a key method for translational studies (4, 5). Far from being controversial, extracellular recordings are currently thriving, undergoing a renewed focus underpinned by the advent of high-resolution multi-electrode mapping (3, 6, 8). A strong future for these important techniques is anticipated.

DISCLOSURES

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AUTHOR CONTRIBUTIONS


REFERENCES


A reply to this has been published concurrently (Sanders KM, Ward SM, Koh SD. Reply to O’Grady et al. Physiol Rev 95: 693–694, 2015. doi:10.1152/physrev.00006.2015).


