Letter to the Editor

REPLY TO O’GRADY ET AL.

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TO THE EDITOR: In our recent review of interstitial cells in smooth muscle function (10), we questioned the value of extracellular recording from visceral smooth muscles without controls for movement, a well-known contaminant of extracellular recordings of biopotentials. In GI muscles, electrophysiologically events (slow waves) are small in amplitude (i.e., <60 mV) and slow to develop (<2 V/s) in contrast to the excitable events of heart, skeletal muscle, and neurons. Slow waves are generated and propagate actively by a relatively small number of cells (interstitial cells of Cajal) buried within smooth muscle tissues. These factors confound the ability to record field potentials, especially when contractile movements overlap these events in time (3). Thus, to validate the recording technique and convince skeptics like ourselves who have performed control experiments on sheets of smooth muscle tissue from four species in vitro, it seems logical, and frankly a matter of scientific necessity, to perform controls very carefully before concluding that signals recorded from visceral smooth muscles with extracellular electrodes are primary recordings of electrophysiologically events. Actually, few studies over the decades have performed controls for movement artifacts, and based on our observations with human, dog, monkey, and mouse gastric muscles, we questioned whether recordings in the literature are valid representations of electrophysiologically events or artifacts of movement. While we have not yet published our studies on dog, monkey, and human muscles, we have presented our findings at international meetings attended by Dr. O’Grady and two of his colleagues. They apparently discount our results and question our ability to record electrical events with surface electrodes. We have reported our techniques and have shown our methods and filtering parameters to be suitable for capturing the kinetics of authentic slow waves in GI muscles (3).

We thought progress was possible when a paper appeared in the Journal of Physiology, in which movement stabilization was attempted in studies of pig small intestine and stomach (2). However, the controls described did not muster confidence, and we commented on the shortcomings in our review. i) Dihydropyridines reduce, but do not block, contractile movements in many GI muscles, if one views the tissues with adequate magnification. No information was provided about the efficacy of these compounds in blocking circular and longitudinal muscle contractions in the pig. ii) We were not concerned with the dose of dihydropyridine administered to the pig but with the concentration effectiveness in blocking contractions of longitudinal and circular muscles. iii) True stabilization of movements does not seem likely in GI muscles in vivo because pulsatile flow of blood, respiration, etc. must still occur. Evidence of these movements is not apparent in the figures provided, so one wonders just how carefully movement was resolved. We have found that movements of <50 μm generate movement potentials similar to the events typically claimed to be slow waves. Thus we are doubtful, from their data, that movements in both layers of muscle (under their electrode arrays) were suppressed.

Early in our communications on this topic, we offered to collaborate with Dr. O’Grady and to perform tests on several species to resolve whether three extracellular recordings are suitable for recordings of slow waves in GI muscles. We believe that proper control experiments must include tests on muscle sheets, in vitro, where slow waves are undisturbed and movements can be stabilized (see suggested protocols in Ref. 3), but such a collaboration has not taken place. We once again extend such an invitation for collaboration to Dr. O’Grady and his colleagues to test electrical recording techniques and parameters they deem ideal on muscle sheets in which motion is stabilized unequivocally and electrical slow waves persist.

Several reasons make it important to determine unequivocally whether extracellular recording provides valid electrophysiologically information. i) Much that we know about whole organ GI electrophysiology, especially in humans, is dependent on whether electrical or mechanical behavior is recorded by this method. For example, classic studies show that human gastric electrical activity occurs at 3 cycles per min (cpm) (6), yet two labs have shown higher frequency slow waves in human gastric muscles when intracellular microelectrode recording was used (5, 9). ii) Extracellular recording is performed on human patients in gastroenterology clinics (1, 4, 7). The technique, called electrogastrography, is used to diagnose electrical abnormalities thought to explain gastric emptying disorders and gastroparesis. Doesn’t it seem imperative to determine whether electrogastrography is a valid clinical procedure or an artifact of complex abdominal movements? iii) Dr. O’Grady and colleagues perform electrical recordings on human patients during abdominal surgery (8). iv) Would the risk-to-benefit ratio for these studies be acceptable if the techniques used to measure GI electrophysiology were not valid?

The best resolution of this controversy, as communicated to Dr. O’Grady in September of 2010, would be to perform rigorous control experiments that satisfy all criticism. We took it upon ourselves to perform such control experiments, and the results left us deeply skeptical about the validity of extracellular recording in visceral smooth muscles and the results and interpretations from many classic studies of GI electrophysiology. Therefore, we conveyed this concern in our review.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES


