



Slow Wave(s) of Enthusiasm: Electrogastrography as an Electrodiagnostic Tool in Clinical Gastroenterology

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The stomach is an electrical organ. Much like in the heart, gastric depolarizations are generated in a ‘pacemaker’ region and are linked to changes in muscle contractility. In the human stomach, these pacemaker depolarizations originate in the proximal stomach and continually and slowly spread toward the pylorus through the smooth muscle syncytium at a rate of approximately three times per minute. The first electrical recordings of these ‘gastric slow waves’ were reported about 100 years ago [1], after the initial descriptions of the interstitial cells of Cajal (ICC) were published. Yet, the mechanisms of gastric slow wave generation by these ICCs and the processes involved in electromechanical coupling of slow waves to smooth muscle contractions took decades of rigorous study to understand in detail [2, 3]. Despite this continued research attention, there are gaps in the understanding of the molecular and electrophysiological basis for numerous patterns of gastric motility. Similarly, the precise pathophysiologic mechanisms driving aberrant ICC function, patterns of gastric slow wave propagation, and electrical-mechanical coherence in several chronic gastric disorders are poorly understood. Clearly, there is no shortage of challenges remaining for the field of neurogastroenterology.

Gastric slow waves can be recorded noninvasively via cutaneous electrodes placed on the abdomen to generate the ‘electrogastrogram’ (EGG). EGG faces a number of technical issues, including the need for significant amplification to detect signals with low amplitudes (generally much lower than 500 μV , and often closer to 50–200 μV), combined with the necessity of filtering competing electrical signals from the heart and other organs, and minimizing respiratory and

other movement artifacts [3]. Many of these basic problems were solved by the early 1980s, ushering in a growing wave of interest in EGG during the late 1980s and the 1990s as a translational tool to noninvasively study gastric activity under a variety of physiological states and in patients with numerous chronic gastric conditions. Several metrics of EGG slow waves arose during this formative time, driven by the development of computerized methods of using spectral analysis of the raw signal to generate visually appealing “spectral frequency-time” plots of the data [4]. More commonly used metrics for EGG analysis include the proportion of time in which the EGG dominant frequency (DF) falls within ‘normogastric,’ ‘bradygastric,’ and ‘tachygastric’ frequency ranges, as well as the proportion of the total EGG power positioned within these categories. Other less commonly metrics included descriptions of the stability of the dominant spectral frequencies over the recording time and changes in dominant power with different states of gastric filling, among others. By the early 2000s, there had been enough collective experience with EGG to propose electrogastrography as a viable electrodiagnostic tool in the clinical evaluation of patients with unexplained nausea and vomiting and/or dyspepsia [5].

Yet, enthusiasm for EGG soon ebbed and has now become nearly non-existent in contemporary gastroenterology practice. What happened to this initial wave of enthusiasm for EGG? Perhaps the complexity of data interpretation and the technical challenges of obtaining high-quality recordings contributed to EGG’s decline. More likely, the fact that EGG findings are not completely deterministic, i.e., gastric electrical activity is an imperfect proxy for actual gastric motility, led to the suspicion that EGG was less clinically useful than other more direct measures of motility such as gastric scintigraphy or antral duodenal motility testing. But did the field abandon EGG prematurely?

In this issue of *Digestive Diseases and Sciences*, Carson et al. present a large meta-analysis and systematic review of the literature measuring EGG in those with chronic nausea

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and vomiting syndromes (gastroparesis, chronic nausea and vomiting syndrome, and cyclic vomiting syndrome, which the authors collectively refer to as 'NVS'), functional dyspepsia (FD), gastroesophageal reflux disease (GERD), and healthy controls (HC) [6]. A rigorous approach was used for this analysis, even if the source literature is older and fairly heterogeneous in methodology. The authors followed PRISMA guidelines, had PROSPERO registration, applied risk-of-bias tools, assessed measures of heterogeneity and publication bias when feasible, and generally had a robust statistical analytic framework to handle mixed forms of reported EGG-derived parameters. The fairly striking conclusion is that 'standard,' low-resolution EGG-derived spectral frequency metrics are considerably shifted in those with NVS and GERD, but much less so in FD, compared with HCs. Thus, EGG methods may yet still have some value as noninvasive biomarkers for stomach disorders.

The differentiation of FD from gastroparesis (GP) has become a newer battleground in neurogastroenterology discussions. One may conceive of both disorders as lying on a continuum of gastric sensorimotor dysfunction, since their clinical presentations have substantial overlap [7, 8]. The problem is that there are few widely available clinical tests other than gastric scintigraphy to help truly differentiate these two disorders. Although impaired fundic relaxation is believed to substantially contribute to the pathophysiology of FD, there are no widely available tests for this aspect of stomach function. Interestingly, since gastric slow waves are much less prominent in the gastric fundus, the EGG reflects myoelectrical activity primarily in the gastric body and antrum. Presumably, impaired fundic relaxation may not have a clear 'EGG phenotype' that is distinct from a normal pattern. The information presented in the Carson et al. study suggests that EGG could be useful to identify subgroups of patients with 'gastroparesis-like syndrome'—those with mechanisms related to abnormal fundic relaxation (perhaps those with a 'normal EGG') or related to antral dysmotility (those with an 'abnormal EGG'). Whether EGG has sufficient pathophysiologic correlates to be able to differentiate these groups and personalize the initial treatment plan in such perplexing patients remains to be evaluated.

Carson et al. also report a surprising result that patients with GERD also have substantial EGG abnormalities, with a higher percentage of time spent in bradygastric and tachygastric frequency ranges than HCs. The degree of the abnormality is even on par with NVS patients. This suggests that GERD may share some mechanisms with gastroparesis, perhaps with some delay in gastric emptying and abnormal gastric pressure gradients. Indeed, gastric prokinetic medications have long been recognized as effective GERD treatments [9]. Perhaps EGG may be useful in the diagnostic evaluation of those with GERD, by identifying patients with

EGG alterations that would suggest initial treatment using prokinetic medications.

What does the future hold for EGG? High-resolution EGG using denser electrode arrays and more advanced signal processing methods is one exciting development that can identify slow wave trajectories and rates of slow wave propagation [10]. Perhaps EGG metrics from these higher resolution studies will provide even more diagnostic precision in those with chronic gastric disorders and identify individualized therapeutic targets. It would seem that another (slow) wave of enthusiasm for EGG in gastroenterology practice is steadily rising. Stay tuned to the correct frequency!

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