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Commentary

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The Stomach, the Mouth, or the Food? The Puzzle of Gastric Emptying

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Introduction

The application of MRI to visualize the tissues of the body has opened a completely new field of digestive research. With the introduction of MRI, the black box that was the stomach, which had been opened slightly by isotope marker detection, scintigraphy, and positron emission tomography (PET), could now be made fully visible. When scanning the gastric tissues using an MRI scanner, we automatically visualize the contents of the stomach as well (1). Given the fact that the products we consume are generally similarly responsive to radiofrequency waves as our tissues are, we can quite clearly visualize the contents and their digestion, in close to real time (**Figure 1**). This has allowed inspection of what is happening inside the stomach after consumption of meals. In order to simplify designs, most stimuli in gastric research have been homogeneous fluids (important to calculate both macronutrient and energy amounts per milliliter of content). This fact may have unintentionally confounded our understanding of gastric emptying, given gastric sieving effects and orosensory effects on gastric emptying as demonstrated by Krishnasamy et al. (2) in this issue of *The Journal of Nutrition*.

Gastric Emptying

One of the main outcome measurements using MRI scans has been simply evaluating how fast the content empties from the stomach. This has quickly been adopted as an interesting technique to relate food qualities to gastric emptying behavior (2, 3), the goal generally being, apart from fundamental understanding, to determine how we can reduce energy intake by enhancing satiety through delayed gastric emptying (4).

Earlier work demonstrated the emptying curve of the stomach to follow an intuitive exponential term function, which has generally held up as more and more MRI data became available (5). Using this curve, we can fit it to our data points and derive a half-emptying time, commonly referred to as a gastric emptying t50 (GE t50), which makes it easy to compare treatments as well as to compare results of different published studies. It should be noted, however, that GE t50 is a highly compounded variable, which only gives broad insight into the complex dynamics of gastric emptying. Depending on the individual paradigm, many other factors such as emptying rate, gastric load, or emptying phase may be more revealing.

Factors Influencing Gastric Emptying

What exactly influences gastric emptying has proven to be somewhat elusive. We know from work in our laboratory, which confirmed earlier reports from Nottingham University (the leading institution in this field), that calorie intake seems to be the main determinant of gastric emptying (6, 7). However, this does not tell the whole story. From other studies, including that presented by Krishnasamy et al. (2), we know that the food form (or food matrix) can influence gastric emptying, even when the stimuli are isocaloric. Mechanistically, the causal link between greater calorie intake and delayed gastric emptying has been relatively well understood in terms of hormonal and neural feedback from the duodenum to the pyloric sphincter and gastric wall. However, the effects of intragastric structure or viscosity on gastric emptying are less clear.

On the one hand, some studies indicate that viscosity does not affect gastric emptying significantly (5, 8) and on the other, there has been work showing some effects of viscosity (3). More importantly, the work by Krishnasamy et al. (2) shows the effect of viscosity (2). The work by Krishnasamy et al. (2) shows the effect of eating whole apples: it delays gastric emptying. Under the current understanding one might expect that pureed apples are more homogeneous than chewed apple parts inside the stomach. In the case of whole apples, one might expect that through gastric sieving the liquid fraction of the mixture may have emptied more quickly from the stomach, lowering the overall GE t50. This was not the case, however, supporting the hypothesis that gastric emptying is delayed by orosensory exposure which may be dependent on the actual chewing of whole foods.

Whole foods, ingested after chewing, have not been studied extensively by MRI, mainly owing to the aforementioned issues concerning homogeneity of stimuli. It remains uncertain how exactly viscosity and orosensory behavior affect gastric emptying. One challenge in this area is that viscosity inherently affects eating behavior, i.e., more viscous materials often require more chewing or, at the very least, they coat the mouth more, thereby increasing orosensory exposure.

Lastly, large particles must be broken down, thereby slowing emptying [e.g., through sieving (9, 10)]. However, small particles

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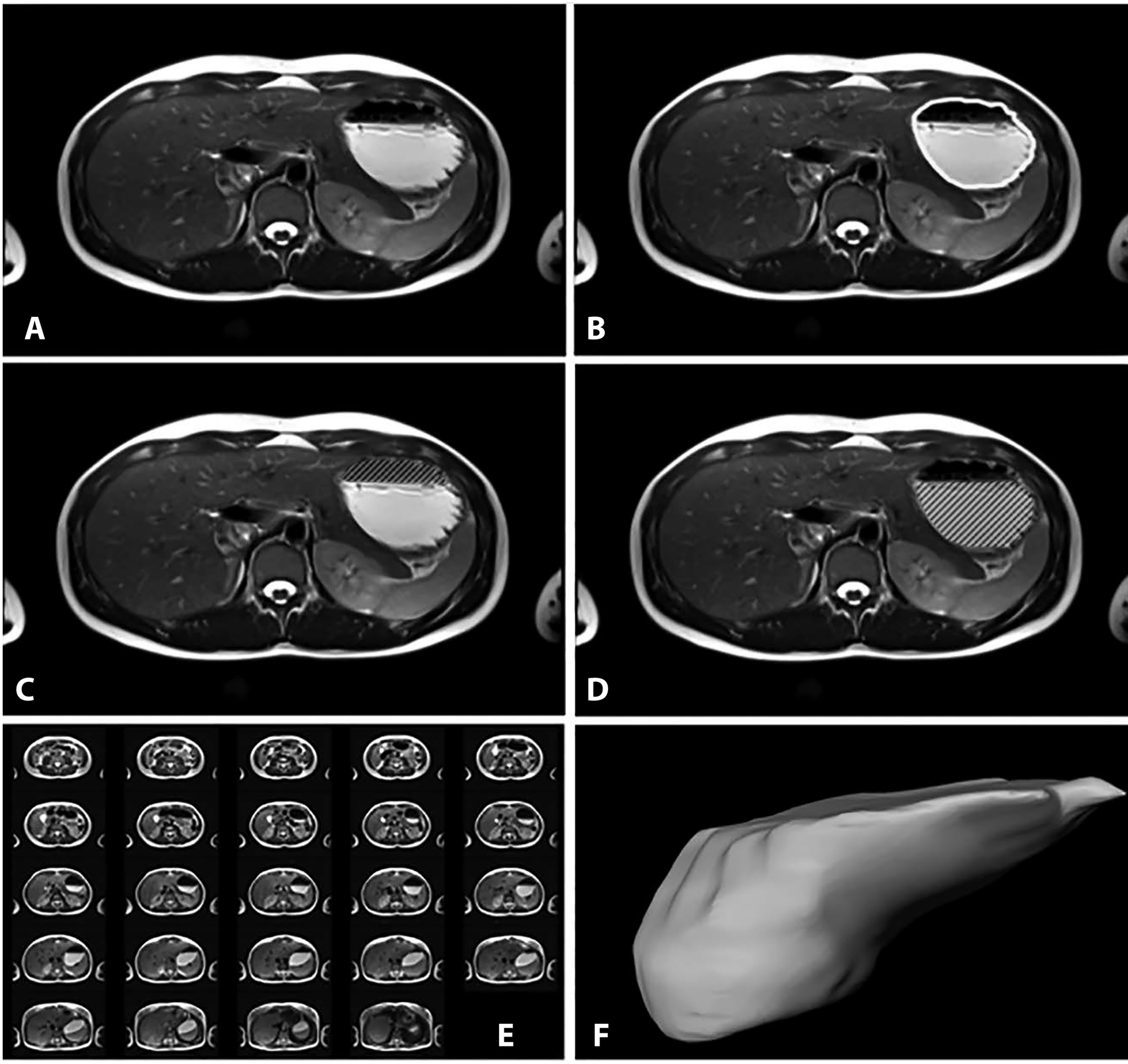

FIGURE 1 Examples of MRI cross-sectional slices of the stomach. (A) Original image, (B) gastric lining highlighted with a white line, (C) air inside the stomach highlighted by diagonal bars, (D) liquid fraction of gastric content highlighted by diagonal bars, (E) overview of all slices of a full scan of the stomach, and (F) 3-D representation of gastric content based on content slices.

may slow emptying by releasing nutrients more quickly. Which of these effects dominates may depend on the specific food and other factors which are not completely understood.

Orosensory

Thus, one of the main questions that warrants a clear answer is the effect of orosensory exposure on gastric emptying, and the subsequent question of whether viscosity/food form is the underlying mechanism or whether the exposure itself is enough to affect gastric emptying.

These questions are not easily tested experimentally. It is difficult to study orosensory exposure specifically without the stimulus subsequently ending up in the stomach and exerting effects. Disentangling the effects is challenging. From recent animal work, we know that mouth flushing may be enough (11), but ideally, we would use procedures such as the use of nasogastric tubes to completely bypass orosensory effects. However, these have their own drawbacks and validity concerns and deviate greatly from normal eating behavior, whereas our goal is to understand normal physiology. It is challenging to find isocaloric, isovolumetric stimuli which allow independent manipulations of viscosity and orosensory exposure. If this orosensory delay of gastric emptying can be convincingly demonstrated in the future, a subsequent question is how this regulation works: whether by hormonal or by direct neural modulation.

Conclusion

The area of MRI and gastric emptying research includes many more avenues not mentioned in this short commentary: correlations with blood markers fMRI research, visceral sensitivity and satiation, and insights into gastric motility. MRI has revolutionized our understanding of the behavior of chyme inside the stomach and the emptying process. Currently we can look even further downstream to the small and large intestine contents. The use of homogeneous fluids as the meal stimulus limited our knowledge of gastric emptying of real foods. Although this is understandable given the context of MRI research, we have known since the seminal article by Haber et al. (10) that food form is of great importance (9): eating an apple or drinking apple juice or a smoothie are not the same in terms of the orosensory experience or the resulting MRI measurements of the stomach.

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