

analysis finding that “the most common cognitive side effect of deep-brain stimulation was a decrement in verbal fluency.^[2] Impaired verbal fluency is characterized by communication difficulties and by problems in generating word lists.” Okun and colleagues also conducted a study that showed that a “decrease in verbal fluency is an effect of surgical electrode implantation, not an effect of stimulation.”³

Did the EARLYSTIM investigators use a technique of lead placement that avoided impairing verbal fluency, or were the tests they used for assessing cognitive outcomes not sensitive instruments for measuring verbal fluency?

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THE AUTHORS REPLY: We agree with Carmona-Torre and colleagues that infections of the electrodes are an important complication of neurostimulation. Most of the infections are skin infections,¹ but they can also extend into the brain in rare cases.² Of the 124 patients in the neurostimulation group in EARLYSTIM, 4 (3.2%) had skin infections, including 2 with intracerebral infection that needed surgical revision of the system. The improvement in quality of life for these 4 patients was in the range of the entire group, and they did not have long-term sequelae. We agree that such infections can cause serious long-term effects and need to be discussed with

the patient as an important risk. It is a challenge to reduce this infection rate with safer implantation techniques and better implants.

Keller raises questions regarding the effect of neurostimulation on verbal fluency shown in all controlled studies.³⁻⁵ We assume that verbal fluency is also significantly worse in patients in the neurostimulation group than in those in the control group in EARLYSTIM. Therefore, we have added a second protocol, EARLYSTIM-speech, to compare standardized speech recordings at baseline and at 24 months. This study will provide more information not only on the frequency and severity of changes of word fluency but also on the effect of these changes on communication in real life.

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Esophageal Sphincter Device for Gastroesophageal Reflux Disease

TO THE EDITOR: In their study, Ganz and colleagues (Feb. 21 issue)¹ found that the effect of an esophageal device on the median percentage

of time in a 24-hour period in which the pH was less than 4 (fraction time) was 3.3%, which is disappointingly near the upper limit of the nor-

mal range, leaving about half the patients with still-abnormal acid reflux. Fundoplication, in turn, yielded a median fraction time of 0.4% after 6 months² and 0.7% after 5 years,³ according to the Long-Term Usage of Esomeprazole versus Surgery for Treatment of Chronic GERD (LOTUS) trial. The early results of the pilot study by Ganz et al. disappoint even more when we take into account the selection of favorable patients by means of excluding those with hiatal hernia, Barrett's esophagus, or grade C or D esophagitis (i.e., mucosal breaks that extend between two or more mucosal folds but involve <75% of the circumference of the esophagus and mucosal breaks involving ≥75% of the circumference of the esophagus, respectively) — all dismal prognostic factors in the treatment of reflux.⁴⁻⁶ Unfortunately, the moderate results in terms of acid reduction were not outweighed by a high degree of safety. The device was removed in 6 patients, including in 3 owing to dysphagia. In contrast, only 1 of the 248 patients who underwent fundoplication in the LOTUS study required more than one endoscopic dilation for dysphagia. We contend that carefully designed prospective, randomized trials are indispensable before the magnetic device can be recommended for routine use in the treatment of gastroesophageal reflux.

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TO THE EDITOR: Ganz and colleagues report the safety and effectiveness of a magnetic device to

augment the esophageal sphincter for the treatment of gastroesophageal reflux disease. Dysphagia requiring esophageal dilation occurred in 19 patients (19% of the cohort), and device removal was required in 6 (6%).

Esophageal motility disorders, including reversible pseudoachalasia, have been reported after placement of laparoscopic adjustable gastric banding for the treatment of morbid obesity¹⁻³ and have been characterized with the use of standard and high-resolution manometry of the esophagus and barium esophagography.

The prevalence of dysphagia in this study, combined with the need for esophageal dilation and device removal in a subset of patients, suggests that the device may induce esophageal motility disorders, including pseudoachalasia. Reporting of the manometric and barium-esophagographic data collected at 1 year, as compared with baseline, and the incidence of esophageal motility disorders, including pseudoachalasia, among patients with postprocedural dysphagia or obstructive symptoms would allow for a more complete assessment of the safety of this device.

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THE AUTHORS REPLY: Miholic and Sporn note that the reduction in esophageal acid exposure after magnetic sphincter augmentation was in the normal range but less than that seen after Nissen fundoplication in the LOTUS trial.¹ However, the LOTUS results are not comparable to those of our study. Our study was limited to patients who either did not have a response to proton-pump inhibitors or had only a partial response, whereas the LOTUS trial excluded those with a partial or refractory response to proton-

pump inhibitors. In our study, 100% of the patients had abnormal pH scores at baseline, as compared with 73% of those in the LOTUS trial, which may indicate that our patients had greater incompetence of the lower esophageal sphincter. This is supported by the fact that the majority of patients in our study (57%) reported either moderate or severe regurgitation at baseline, as compared with the LOTUS trial, in which the majority (68%) reported either no regurgitation or only mild regurgitation.

In our study, a significant reduction in esophageal acid exposure was achieved. At baseline, the median total percentage of time with acid exposure was 10.9%, which dropped to 3.3% at 1 year of follow-up ($P < 0.001$). This significant reduction in esophageal acid exposure is indicative of an improved antireflux barrier, which translated into substantial symptom improvement, discontinuation of proton-pump inhibitors, and patient satisfaction for the majority of study patients at 3 years of follow-up. It is the totality of the clinical outcomes, not a single physiological factor such as pH measurement, that forms the basis for evaluating the effectiveness of a treatment. Acid in the distal esophagus does not indicate volume reflux, whereas regurgitation is a symptom of sphincter failure and volume reflux. Three years after implantation, only 1% of our patients had moderate or severe regurgitation, as compared with 57% at baseline.

The incidence of postprocedural dysphagia in our trial was similar to that in the LOTUS trial (and other fundoplication studies).¹⁻³ It is unclear how these two trials compare with regard to dilations, since the LOTUS trial allowed one dilation per patient and counted only patients who under-

went more than one dilation, whereas we reported all dilations.

Murphy and Kearney inquire about postprocedural manometric abnormalities or motility disorders related to the magnetic sphincter device that are similar to those reported after Nissen fundoplications.⁴ At 1 year, all our patients were evaluated with the use of manometry and barium esophagography, and we did not observe any clinically meaningful manometric changes from baseline or pseudoachalasia after magnetic sphincter augmentation. These results are reported in the Supplementary Appendix, available with the full text of our article at NEJM.org.

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Vitamin B₁₂ Deficiency

TO THE EDITOR: In the review article describing vitamin B₁₂ deficiency (Jan. 10 issue),¹ Stabler states that vitamin B₁₂ is known as cyanocobalamin in the United States and hydroxocobalamin in Europe. As a result of a subgroup analysis of U.S. and European patients with renal impairment in the Vitamin Intervention for Stroke Prevention (VISP) trial,² it has been proposed³ that these two forms of vitamin B₁₂ are not clinically equivalent. The confounding effect that resulted

when the European patients in the trial received methylcobalamin and the U.S. patients received cyanocobalamin may have influenced this trial result.³ Stabler also states that high-dose oral vitamin B₁₂ tablets are as effective as intramuscular monthly injections in correcting blood and neurologic abnormalities. However, patients with renal failure who are given cyanocobalamin accumulate cyanide, which can antagonize the beneficial homocysteine-lowering effects and asym-