ther intracranial injections nor infusions of the saline vehicle significantly altered gastric acid output (Fig. 1). The stimulation of acid secretion caused by intracranial injections of pentagastrin was abolished by subdiaphragmatic vagotomy (two rats) and by atropine sulfate (0.3 mg/kg, subcutaneously; two rats), suggesting that the response was mediated by vagal parasympathetic fibers to the stomach.

Since pentagastrin is a potent secretagogue when injected systemically in the rat (*5*) and since vagal blockade also reduces the secretory response to systemic injections of gastrin (*6*), we were concerned that the stimulation of acid secretion in our experiments might have been caused by peptide leaking from the brain into the bloodstream. To test this directly, we implanted catheters in the jugulars of rats that had shown a consistent secretory response to intracranial injections. A dose of 100 pmole of pentagastrin, which potently stimulated acid output when injected intrahypothalamically in these animals, had no significant effect when injected intravenously (Fig. 1). Only intravenous injections of doses 10 to 100 times larger caused effects similar to those caused by 100 pmole injected intracranially.

Figure 2 shows an example of a hypothalamic cannula placement where injection of pentagastrin stimulated acid output. Injections of the same dose into other brain sites, including the lateral cerebral ventricles and caudate-putamen area, failed to increase gastric acid secretion. These results are consistent with those of Manaker *et al.* (*7*), who found that even higher doses of pentagastrin injected into the ventricular system did not increase acid output. Furthermore, in two of our rats in which the intracranial cannulas barely missed the lateral hypothalamus (one about 2 mm anterior and one about 1 mm medial), injections of pentagastrin also failed to increase gastric acid secretion. Similarly, no such increases were observed in two rats in which the hypothalamic cannulas were too ventral, puncturing the base of the brain so that injected pentagastrin entered the subarachnoid space. These results suggest that the lateral hypothalamus may be uniquely sensitive to this action of pentagastrin in the forebrain.

Like the pentapeptide fragment, intrahypothalamic injections of 95 percent pure porcine gastrin also increased gastric acid secretion. In eight animals in nine experiments, the acid output after injection of 100 pmole of porcine gastrin was 44.6 ± 5.3 μEq per 15 minutes compared to 20.6 ± 3.4 μEq per 15 minutes when the same rats were injected with the saline vehicle ($P < .05$). On the other hand, intrahypothalamic injections of the same dose of other peptides common to the gut and brain, including neurotensin, substance P, and vasoactive intestinal polypeptide, failed to alter gastric acid secretion. In fact, bombesin, the amphibian peptide recently found in mammalian gut and brain and known to stimulate acid secretion when injected systemically (*8*), actually reduced gastric acid output from 24.7 ± 3.4 to 4.2 ± 1.3 μEq per 15 minutes ($N = 6$, $P < .05$) when injected into the lateral hypothalamus. Therefore the stimulation of gastric acid secretion by peptides in the hypothalamus appears to be specific to gastrin-like substances.

These observations demonstrate that gastrin can increase gastric acid secretion by acting on the hypothalamus as well as on the stomach. It is uncertain whether circulating gastrin could stimulate the brain sites implicated in our experiments, since it is controversial whether such peptides can cross the blood-brain barrier (*9*). Preliminary findings, however, suggest that intracarotid infusions of pentagastrin in sheep are more potent than intravenous infusions at inhibiting motility of the reticulum of the stomach (*10*). Alternatively, our results also support the idea that gastrin endogenous to the hypothalamus, perhaps acting as a neurotransmitter or neurohormone, participates in the neural control of gastrointestinal function. Since gastrin has been identified in the medulla and in fibers and terminals of the vagus nerve (*2*), it is conceivable that a gastrinergic pathway connecting the hypothalamus and the vagal nuclei and projecting to the gut could be an important component of the neural mechanisms controlling digestion.

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References and Notes

1. J. F. Rehfeld, *Nature (London)* **271**, 771 (1978).
2. _____, N. Goltermann, L.-I. Larsson, P. M. Emson, C. M. Lee, *Fed. Proc. Fed. Am. Soc. Exp. Biol.* **38**, 2325 (1979).
3. F. P. Brooks, *Prog. Gastroenterol.* **3**, 373 (1977); M. Kadekaro, C. Timo-Iaria, M. del M. Vicentini, in *Nerves and the Gut*, F. P. Brooks and P. W. Evers, Eds. (Slack, Thorofare, N.J., 1977), p. 377.
4. The gastric cannula (inner diameter, 5 mm; length 15 mm) was similar to that described by R. C. Young, J. Gibbs, J. Antin, J. Holt, and G. P. Smith [*J. Comp. Physiol. Psychol.* **87**, 795 (1974)].
5. A. M. Barrett, *J. Pharm. Pharmacol.* **18**, 633 (1966).
6. M. I. Grossman, *J. Physiol. (London)* **157**, 14P (1961); S. Emas and M. I. Grossman, *Am. J. Physiol.* **212**, 1007 (1967).
7. S. Manaker, S. H. Ackerman, H. Weiner, *Physiol. Behav.* **23**, 395 (1979).
8. G. Bertaccini, V. Ersparmer, P. Melchiorri, N. Sporanzi, *Br. J. Pharmacol.* **52**, 219 (1974).
9. E. A. Cornford, L. D. Braun, P. D. Crane, W. H. Oldendorf, *Endocrinology* **103**, 1297 (1978).
10. H. W. Chapman, W. L. Grovum, J. C. Newhook, *Ann. Rech. Vet.* **10**, 200 (1979).
11. Supported by the Medical Research Council of Canada. We thank E. Potter and B. Soper for technical assistance, M. I. Grossman for his gift of porcine gastrin (G-17-1), and V. Mutt for his gift of vasoactive intestinal polypeptide (the synthetic peptides neurotensin, substance P, and bombesin were purchased from Peninsula Laboratories). A preliminary version of this report was presented at the 80th Annual Meeting of the American Gastroenterological Association, New Orleans, May 1979.

2 May 1980

Holographic Assessment of Microwave Hearing

Human beings with normal audiograms can "hear" pulsed microwaves; they perceive a clicking or popping sound each time a suprathreshold, 1- to 30-μsec pulse is incident on the head (*1*). While the quantity of energy absorbed per pulse at the threshold of hearing is small (~ 20 μJ/g), as is the resulting increment of average temperature, ~ 5×10^{-6} °C (*2*), most investigators of this phenomenon believe that the hearing is due to thermoelastic expansion (*3*); that is, one hears because a minuscule wave of pressure is set up within the head when the absorbed microwave pulse is converted to thermal energy (*4*). Frey and Coren (*5*) challenge the thesis that thermoelastic expansion of the skull or soft tissues of the head is critical to microwave hearing. Using a time-averaged laser-holographic procedure during pulsed irradiation of dead rats and guinea pigs, they failed to find evidence of thermoelastic displacement in serially exposed scalp, skull, and brain. They then argue (i) that thermoelastic events in these structures are not responsible for microwave hearing and (ii) that thermoelastic events within the cochlea probably are. We show that methodological and conceptual errors reduce both of these arguments to non sequiturs.

Frey and Coren (*5*) claim that their holographic technique is sensitive to vibratory displacements on the order of 6×10^{-8} m. They do not indicate (i) that this level of sensitivity is achieved only in measurement of a continuous, undamped vibration (*6*); (ii) that the putative sonic wave launched in the head by a microwave pulse is a rapidly damped transient that persists for less than 300 μsec (*7*), which would reduce the sensitivity of their technique well below the level claimed (*8*); or (iii) that the energy

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content of their microwave pulses ranged just above the auditory threshold (*2*). Von Bekesy (*9*) has shown that the auditory threshold for vibratory displacements of the human skull at frequencies near 5 kHz, which characterize the acoustic transient, lies between 10^{-11} and 10^{-10} m (*9*, p. 173). It is easy to see why Frey and Coren found no evidence for thermoelastic expansion; they were attempting to measure vibrations at amplitudes 1,000 to 10,000 times smaller than their method could, at best, resolve.

Frey and Coren report that their holographic technique recorded displacements in materials such as foamed plastic loaded with amorphous carbon, but they do not point out that, per unit of absorbed microwave energy, the elastic and expansive properties of these materials yield displacements that are much greater than are those of biological materials and that the duration of vibration is also quite long (*2*). They also report that vibrations were detected holographically in serially exposed muscle, skull, and brain of a dead guinea pig when a buzzer 10 cm distant produced airborne sound at a pressure level of 50 dB. The displacements induced in any of these tissues by such a weak sonic field would be less than 10^{-10} m (*10*), which is well below the maximum sensitivity of their holographic measure, even for a continuous, undamped wave. Either the pressure level of their airborne sound was much higher than 50 dB or, perhaps, their buzzer was mounted on a solid, elastic medium such as a laboratory bench that more efficiently transmitted artifactual vibration to the guinea pig or to the holographic apparatus.

Frey and Coren conclude that thermoelastic expansion within the cochlear apparatus "probably" underlies microwave hearing, but do not explain how microwave energy can be absorbed in, and move, the cochlear apparatus without also being absorbed in and moving the scalp, skull, and other tissues that surround the cochlear apparatus. Their conclusion is not supported by data. In an earlier paper in which Frey (*11*) argued exactly the reverse, namely, that the cochlea is not activated by microwaves, he also based his conclusion on a failure to find the effect he was looking for.

Frey and Coren offer nothing to disconfirm the anatomically general thermoelastic hypothesis; given the insensitivity of their technique, their failure to detect microwave-induced displacements is simply not pertinent to the question they raise. The hypothesis that microwave hearing is a sequela of anatomically generalized thermoelastic events in the head is appealing, not only because of an abundance of supporting theory and data (*12*), but also because it is falsifiable. Dispassionate efforts to falsify an hypothesis are both desirable and legitimate, but must be undergirded by competent methodology.

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References and Notes

1. A. H. Frey and R. Messenger, Jr., *Science* **181**, 356 (1973); J. C. Sharp, H. M. Grove, O. P. Gandhi, *IEEE Trans. Microwave Theory Tech.* **22**, 583 (1974); V. V. Tyazhelov, R. E. Tigranian, E. O. Khizhniak, I. G. Akoev, *Radio Sci.* **14** (6S), 259 (1979).
2. A. W. Guy, C. K. Chou, J. C. Lin, D. Christensen, *Ann. N.Y. Acad. Sci.* **247**, 194 (1975).
3. K. R. Foster and E. D. Finch, *Science* **185**, 256 (1974); D. R. Justesen, *Am. Psychol.* **30**, 391 (1975); C. K. Chou, A. W. Guy, R. Galambos, in *Biological Effects of Electromagnetic Waves*, C. C. Johnson and M. L. Shore, Eds. [HEW Publ. (FDA) 77-8010, Washington, D.C., 1977], p. 89; R. M. Lebovitz and R. L. Seaman, *Radio Sci.* **12** (6S), 229 (1977); D. E. Borth and C. A. Cain: *IEEE Trans. Microwave Theory Tech.* **25**, 944 (1977); J. C. Lin, *Microwave Auditory Effects and Applications* (Thomas, Springfield, Ill., 1978).
4. R. M. White, *J. Appl. Phys.* **34**, 2123 (1963); *ibid.*, p. 3559.
5. A. H. Frey and E. Coren, *Science* **206**, 232 (1979).
6. M. Zambuto and M. Lurie, *Appl. Opt.* **9**, 2066 (1970).
7. C. K. Chou, A. W. Guy, R. Galambos, *Radio Sci.* **12** (6S), 221 (1977).
8. The magnitude of vibratory displacement as determined by the time-averaged holography is indexed by the degree of dimming of the reconstructed image of a vibrating body according to the formula [see (*6*)]

$$\frac{B(\mathrm{m})}{B_0(\mathrm{m})} = \left|\frac{1}{T}\int_0^T \exp\left[j\frac{4\pi}{\lambda}\cdot x_\mathrm{m}(\mathrm{t})\right]dt\right|^2$$

where point m on the surface of an object is displaced by $x_\mathrm{m}(\mathrm{t})$ from its equilibrium position during the exposure of the hologram, $B(\mathrm{m})$ is radiance at the point m, $B_0(\mathrm{m})$ is radiance in the absence of vibration, T is exposure time, and λ the wavelength of the laser beam. For a steady sinusoidal oscillation of point m with amplitude of $\lambda/10$, the brightness of the reconstructed image is reduced by approximately 1/2, leading to the sensitivity claimed by Frey and Coren. For transient vibration with very small duty cycle ($n\tau << 1$), the brightness decrease in the reconstructed image becomes

$$\frac{B(\mathrm{m})}{B_0(\mathrm{m})} \cong \left|n\int_0^\tau \exp\left[j\frac{4\pi}{\lambda}\cdot x_\mathrm{m}(\mathrm{t})\right]dt + 1 - n\tau\right|^2$$

where n is the number of vibratory inducements (that is, microwave pulses) per unit time and τ is the effective duration of the transient vibration per vibratory inducement. For a short transient vibration, since the integral approaches 0 and $B(\mathrm{m})/B_0(\mathrm{m}) \rightarrow 1$, it is difficult to get detectable dimming of the hologram. This analysis shows that the time-averaged holographic technique is insensitive to transient vibration.
9. G. von Bekesy, *Experiments in Hearing*, E. G. Wever, Transl. (McGraw-Hill, New York, 1960).
10. Compare von Bekesy (*9*, chap. 6) with *Reference Data for Radio Engineers* (Sams, New York, 1968), chap. 35.
11. A. H. Frey, *IEEE Trans. Microwave Theory Tech.* **19**, 153 (1971).
12. See the recent review by J. C. Lin, *Proc. IEEE* **68**, 67 (1980).

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When an object vibrates sinusoidally in time-average holography, it spends most of its time near its two positions of maximum displacement, where its velocity is zero—a situation akin to a two-exposure holographic interferogram (*1*). Chou *et al.* (*2*) use this fact, a flat plate model of the head, and their interpretation of their cochlear microphonic data as the basis of their comment. Apparently, they do not realize that such a time-averaged hologram is a special case, because their reference to holography is from the early days of holographic interferometry (*3*). Most of the data in this field have been gathered since 1970 and show that various nonsinusoidal vibrations, such as they assume, can be detected; and they can be described, for example, by the Jacobian elliptic functions $C_\mathrm{n}(\omega t/m)$ and $S_\mathrm{n}(\omega t/m)$, which are solutions to Duffing's equation [see (*1*)].

Further, Chou *et al.* have assumed (*2*) that the head is a flat plate (*4*). The head is actually a complex nonhomogenous mass which will display nodal patterns that are not in agreement with the classical theory of vibrating plates which they assume. It has been demonstrated that such patterns are combinations of classical modes (*5*). Inspection of such holograms shows that the effects of vibrations are exaggerated in the holographic image compared to the oversimplified flat plate model of Chou *et al.* Thus, their analysis is faulty and their conclusion about the sensitivity of the method is not supported, even if we momentarily accept their interpretation of their cochlea microphonic data; data that we showed by other means are apparently due to an artifact (*6*).

Chou *et al.* ignored the critical issue that we raised (*7*), that their cochlea microphonic data are due to an artifact. This did not involve questions of holographic method sensitivity. We questioned the cochlear microphonic experiments of Chou *et al.* because of their use of a foamed plastic support for the ani-

mal's head and a carbon electrode in contact with the round window of the cochlea during microwave exposure. Our experiments and other evidence had shown that microwave pulses could easily vibrate both carbon and foam. We suggested that the data of Chou *et al.* may have been confounded by one or both of these artifacts. Nowhere in their comment do they reply to this critical finding (*8*). In fact, they admit that foamed plastic and carbon materials would "yield displacements that are much greater than are those of biological materials. . . ." Thus, they acknowledge that their microphonic data, the fundamental support of the hypothesis, may be due to an artifact (*9*).

Their commentary misleads also because they state: (i) "Frey and Coren conclude that thermoelastic expansion within the cochlear apparatus 'probably' underlies microwave hearing. . . ." What we in fact said was, "Among the many mechanisms in the cochlea that might account for the perception of microwave energy, consideration should be given to the possibility of thermoacoustic expansion within the cochlea." And (ii), "In an earlier paper [Frey argued] that the cochlea is not activated by microwaves." Frey actually said the reverse may be the case (*7, 10*). Frey is honored, though, that Chou *et al.* acknowledge that, if warranted, he would willingly discard an old hypothesis in the light of new data.

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References and Notes

1. C. M. Vest, *Holographic Interferometry* (Wiley, Toronto, 1979).
2. C.-K. Chou, A. W. Guy, K. R. Foster, R. Galambos, D. R. Justesen, *Science* **209**, 1143 (1980).
3. See their reference 6, which was published in 1970. Stetson [K. A. Stetson, in *Holographic Nondestructive Testing*, R. K. Erk, Ed. (Academic Press, New York, 1974), p. 182] states: "The first hologram of a vibrating object was made on December 4, 1964." He also states: "To date [1974], very little application has been made of hologram interferometry to nonlinear vibration problems, but we may expect this to increase in the future."
4. This is similar to their earlier calculations on thermoacoustic expansion using a tank of water to represent the head and a hydrophone to represent the auditory system from which they concluded that such expansion in the brain, via bone conduction, is the mechanism for microwave hearing.
5. N. E. Molin and K. A. Stetson, *J. Opt. Soc. Am.* **60**, 1378 (1970); *Optik* **33**, 399 (1971); K. A. Stetson, *Appl. Opt.* **11**, 1725 (1972); A. D. Wilson, *J. Opt. Soc. Am.* **60**, 1068 (1970); ——— and D. H. Strope, *ibid.*, p. 1162; A. D. Wilson, *ibid.* **61**, 924 (1971).
6. In their equation, they assigned values to τ and ($n\tau << 1$) that have been derived from their microphonic data—data apparently due to an artifact. Thus, their calculation and conclusion are not valid on that basis alone.
7. A. H. Frey and E. Coren, *Science* **206**, 232 (1979).
8. They also do not reply to four of the other independent lines of evidence published by others that we discussed in calling into question the thermoacoustic expansion-bone conduction hypothesis.
9. Chou *et al.* used their thermoacoustic expansion-bone conduction hypothesis to interpret their microphonic data in such a way that microwave pulses must generate pressure waves in the delicate tissues of the brain that pass into the skull, thence through the muscle of the head, thence through the skin, where it is radiated into the ear canal; then the waves, via air vibration, move the tympanic membrane, the ossicles, and then the oval window of the cochlea. The losses due to mismatches and attenuation in passing through all those interfaces would be substantial, so the initial wave would have to be large.

   Yet Chou *et al.* assume that the tissue displacement induced is so small that it is about one-thousandth (0.001) of the thickness of a cell membrane—a displacement supposedly propagated via the pathway and with the losses noted above. One of the simpler explanations for their data is that the microwave pulses are moving their carbon electrode which is at the round window of the cochlea. Another is if there can be thermoacoustic expansion in the brain, why not in the basilar membrane of the cochlea, as White suggested to us and we cited [see reference 22 in (*7*)]. That would require much less power to induce hearing than the tortuous path to the basilar membrane that they postulate.
10. A. H. Frey, *IEEE Trans. Microwave Theory Tech.* **19** (No. 2), 153 (1971).

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