periments with cats, stereotactically placing the probe within 3 or 4 mm of the third nerve nucleus on the right side. Thermocouples were attached to the refrigeration probe at 1 and 3 mm away from the tip. We then photographed the cat's eyes before, during, and after the temperature of the probe was lowered to about 5°C (Fig. 1, right). We did not reduce the temperature of the probe to 0°C for fear of producing irreversible lesions about the tip of the probe. (*2*). Bright illumination of both pupils was constantly maintained throughout the experiments. Within 20 seconds, the ipsilateral pupil fully dilated and the contralateral pupil partially dilated. Within 45 seconds after the probe was turned off, the pupils returned to normal size. This process of cooling and warming was repeated in each cat at least three times (with cooling periods of up to 10 min) without altering the physiological results or time course of the localized brain cooling. In three cats with similar electrode placements near the third nerve nucleus, the results obtained were exactly the same.

For clinical use, Cooper and his associates (*3*) have introduced a small balloon into the tip of their brain probe. They feel that they can make temporary brain lesions by expanding the balloon and mechanically compressing brain tissue within the thalamus and basal ganglia. They have used this successfully in many hundreds of cases. The expanded balloon, however, has caused hemorrhage in some clinical cases, and thus, whether it can produce temporary lesions within the brain safely is in some doubt. Procaine injections have also been used to produce temporary interruptions of brain function in man. The injection of procaine into the thalamus or basal ganglia has two disadvantages. First the diffusion of a liquid in the center of the brain mass is somewhat unpredictable, and the physiological results of such interruptions are difficult to interpret. Secondly, the seepage of procaine or other local anesthetic agents into the brain ventricles may produce a clinical catastrophe. The use of a single beam of ultrasound for the production of reversible brain lesions has been described (*4*). This is an expensive and complicated tool for routine clinical use, and in experimental work it precludes the use of electrical recording devices at the site of the intended lesion. It is, however, another promising method of producing reversible brain lesions.

Although the brain tolerates heat very poorly (irreversible lesions can be made in the brain substance by heating it to 55° or 60°C), cold is tolerated more readily. The entire body temperature during surgery has been reduced to as low as 10° or 15°C for more than 44 minutes without discernible impairment in brain function (*5*). A localized decrease in brain temperature and its effect on conduction times and somatic and synaptic potentials will be a subject of continuing investigation in this clinic. We are also attempting to build a more slender semiconductor probe for brain cooling (*6*).

Note added in proof: It has come to our attention that a cooling probe was used to make lesions in the cerebral cortex of cats by Balthasar in 1957 [E. Balthasar, *Deut. Z. Nervenheilk.* **176**, 173 (1957)].

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19 June 1961

Functional Effects of Focused Ultrasound on Mammalian Nerves

Abstract. Differential blocking of conduction in mammalian nerve fibers has been produced by irradiation of the whole nerve with focused ultrasound. The smallest (C) fibers are the most sensitive; the largest (A-alpha) fibers are the least vulnerable. Fully reversible blocking can be obtained with carefully graded doses of ultrasound.

Studies of frog sciatic nerve have revealed that the alpha, beta, and gamma fibers in the nerve are differentially sensitive to focused ultrasound (*1*). The effects of ultrasound upon fibers in a wider size range have now been investigated (*2*), in studies of the saphenous nerve of the cat. This is a skin nerve containing the alpha and delta subgroups of the A fibers (with diameters of 6 to 14 and 1 to 5 μ, respectively) and a good representation of C fibers (of 1 μ or less).

In cats anesthetized with pentobarbital sodium, the saphenous nerve was exposed for 8 to 10 cm. Near its origin in the upper thigh and in the middle of the leg it was severed and freed from surrounding connective tissue, so that it could be lifted on stimulating and recording electrodes. Ultrasound (*3*) was directed at the midportion of the nerve. The ultrasound was administered in pulses of 0.4- to 0.9-second duration with a 2- to 3-second interval between pulses.

Action potentials were recorded monophasically and after amplification were displayed on an oscilloscope. In each experiment the intensity (plate voltage of the ultrasonic generator) and duration of irradiation were increased gradually until alterations in the action potentials were noted. Before each irradiation several compound action potentials, with alpha, delta, and C fiber deflections, were photographed as controls. Records were also taken during the period of irradiation and afterwards during recovery from it.

As in the experiments on frog nerve fibers (*1*), it was found that focused ultrasound would abolish conduction of impulses completely and irreversibly if irradiation was sufficiently intense or prolonged. Fully reversible effects could be obtained with graded doses of lower intensity. Experiments were devoted chiefly to producing differential blocking of fibers of different sizes. To this end the administration of ultrasound was deliberately varied in order to explore the effects of different combinations of intensity, duration, pulse interval, and train length.

Figure 1 illustrates the results obtained in one of the most successful attempts to block differentially. Four columns of records are shown (Fig. 1, *A* to *D*). The upper and lower pairs of tracings in each were obtained before and after irradiation, respectively. The upper channel in each pair was recorded at high amplification.

Figure 1, column *A*, shows the effect of a train of 20, 0.5-second pulses of ultrasound at a plate voltage of 700. The C fiber deflection (*4*), indicated by the arrow, in the upper tracing was abolished during the course of this ir-

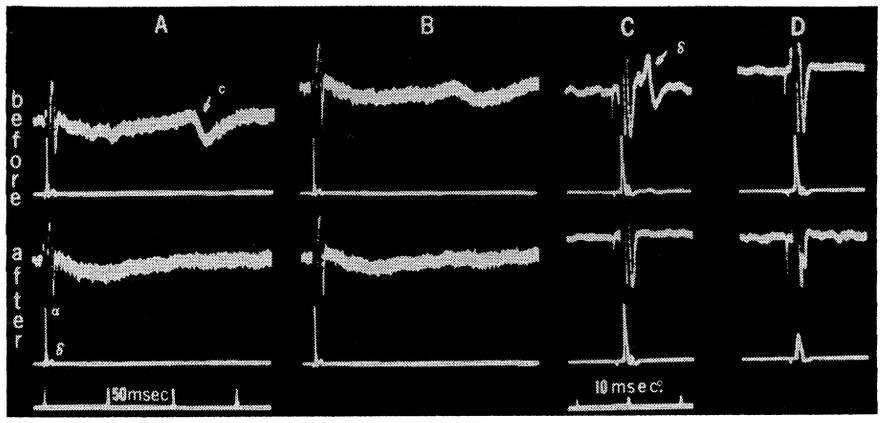

Fig. 1. Oscillographic records of compound action potentials in the saphenous nerve of the cat, showing the effects of irradiation of the nerve with focused ultrasound. The tracings in columns *A* to *D* were photographed at four different times in the course of a series of irradiations. The upper pair of tracings in each column were obtained before, the lower pair after, particular irradiations which blocked conduction differentially. In each pair the upper record is at higher gain. The arrows in columns *A* and *C* indicate the action potentials of C fibers and delta fibers, respectively.

radiation, but there was no alteration in the alpha and delta deflections shown on the lower channel.

The upper pair of action potentials in column *B* were recorded 19 minutes after those in column *A*, and they show recovery of a few C fibers. Twenty additional pulses of ultrasound at this time produced permanent blocking of all C fibers. Again there was no change in the alpha and delta deflections.

Between the records in columns *B* and *C*, 11 additional series of irradiations, comprising 400 pulses at increasing intensities and durations, were administered. The delta fiber deflection (arrow), recorded with a faster sweep in column *C*, was somewhat diminished by this irradiation. At this point 20 0.7-second pulses at a plate voltage of 800 were administered. The delta response was permanently abolished by this more intense irradiation, but the alpha response remained unchanged (*5*).

Between the records in columns *C* and *D*, 160 more pulses of still longer duration were administered without apparent effect on the alpha deflection. The reduction in alpha response seen in column *D* was produced by 60 0.8-second pulses at a plate voltage of 800.

As illustrated by this experiment, there is an inverse relationship between fiber size and vulnerability to ultrasound in mammalian peripheral nerves. It was, however, seldom as clear-cut as in Fig. 1. Although small fibers were most sensitive to irradiation in all experiments, the degree of differential block varied considerably, and the ranges of dosage to which the different groups of fibers were sensitive often overlapped. Irradiation sufficiently intense to block C fibers usually affected conduction in some delta fibers as well. The alpha fibers were always most resistant. In general, the relationship between dosage and blocking was fairly linear throughout any one experiment, but the dosage levels required to produce equivalent effects in different experiments varied considerably. The inconsistencies were too large to be accounted for by biological variability. An explanation is being sought in further investigations of the physiological basis of ultrasonic blocking.

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2. This investigation was supported by research grant No. B-970 from the National Institutes of Neurological Diseases and Blindness and by a research grant (DA-49-007-MD-523) from the Department of the Army to Dr. H. T. Ballantine, Jr., Massachusetts General Hospital.
3. The ultrasound (1.0 Mcy/sec) was generated piezoelectrically by excitation of a quartz crystal and focused with a polystyrene lens. It was transmitted through a saline-filled cone covered by a latex membrane into degassed mineral oil covering the nerve [S → T. F. Hueter, H. T. Ballantine, Jr., W. C. Cotter, *J. Acoust. Soc. Am.* **28**, 192 (1956)].
4. The conduction speed of the fastest C fibers was found to be approximately 1 m/sec at 37°C.
5. The small deflection immediately following the alpha response in the lower records in Fig. 1 was caused by double firing of a few alpha fibers. It resulted from the intensity and duration of the stimulus required to excite the C fibers.

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Gonadotrophic Hormones Affect Aggressive Behavior in Starlings

Abstract. Injections of gonadotrophic hormones into subordinate male European starlings produced reversals in social rank, suggesting that pituitary gonadotrophic hormones rather than gonadal hormones influence aggressive behavior in this species.

The effects of gonadal hormones on the reproductive behavior of animals have been extensively studied (*1*). These hormones, androgens from the testes and estrogens from the ovaries, generally have proved to be very important in determining the characteristic behavior of each sex. Furthermore, the male hormone has long been recognized as a major determinant of aggressive behavior in animals (*2*).

In the European starling, *Sturnus vulgaris*, however, androgens apparently do not play a major role in determining aggressive behavior. Davis (*3*) found that castrated male starlings in the laboratory maintained song and fighting behavior for as long as a month after castration and, furthermore, that the social rank of individual starlings in the group was not affected by injections of testosterone. In addition, Hilton (*4*) and I (*5*) noted that there is a discrepancy between the yearly behavioral and gonadal cycles in male starlings. That is, both the weights of testes and the intensity of aggressive behavior reach a high point during the spring breeding season, and then decline during the summer. But aggressive behavior increases again in the fall even though gonadal weights remain at their minimal summer level. The apparent lack of relationship between androgen levels and aggressive behavior led to the investigation of behavioral effects of other hormones, and, as part of a more comprehensive study of pituitary activity in starlings, to an investigation of the effects of injected commercial gonadotrophins on aggressive behavior of caged male starlings, both intact and castrated (*6*).

In the first series of experiments, groups of five or six birds were placed together in a large flight cage and left together until a clear-cut social rank was evident (about 1 week). Then the lowest-ranking members of the group were given daily injections (for about 2 weeks) of Armour mammalian luteinizing hormone (LH). Administration of this hormone sometimes resulted in increased aggressiveness in the subordinate birds, but rarely in any increase in social rank. It was postulated