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CONDUCTION VELOCITY IN NERVE EXPOSED TO A HIGH MAGNETIC FIELD

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SUMMARY PAGE

THE PROBLEM

Numerous reports in the literature describe changes in the cardiovascular and central nervous systems during exposure to high magnetic fields. Data are either lacking or contradictory from investigations designed to explore these changes at a more basic level. Electrophysiological studies of this type are prerequisite to a better understanding of nervous system function in a magnetic environment, however, and conduction velocity measurements are an informative, initial step toward that understanding.

The vector characteristics of magnetic fields are well known, but their relationship to the effects of magnetic fields on the nervous system has not been established. Once this relationship is determined, insight into the physicochemical nature of biomagnetic effects should follow.

FINDINGS

Action potentials were recorded from frog sciatic nerves exposed to a constant magnetic field of 11.6 kilo-oersted. Electrodes arranged in pairs on segments of nerve oriented parallel and perpendicular to the field permitted conduction velocity measurements to be expressed as a function of field orientation. An increase in conduction velocity was observed to be orientation dependent as was a latent period in its appearance. An aftereffect was noted that persisted to the end of the experiments. Possible mechanisms of action of the field are discussed in terms of current theories of impulse propagation.

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INTRODUCTION

One important aspect of man's interaction with his environment of the future may be his ability to tolerate magnetic fields that are higher in intensity than those normally found at the Earth's surface. An increasing number of reports are in general agreement that high magnetic fields can cause functional changes in the cardiovascular and central nervous systems (1-4). This is not true, however, of the more basic neurophysiological studies where the results are limited in number and contradictory in nature.

As early as 1879, McKendrick (5) noted contraction of frog gastrocnemius muscle when the sciatic nerve was exposed to a magnetic field. Drinker and Thomson (6), however, were unable to detect any changes in irritability or conductivity of nerve exposed to fields reaching 18,725 cgs lines per square centimeter. Most of the more recent studies have been conducted by the Soviet investigators. Liberman et al. (7) cited studies by Petrov and by Erdman in which alterations in the rheobase and chronaxie of frog nerve were observed after exposure to a constant magnetic field. Liberman's group was unable to confirm these findings in nerve exposed to fields of 10 kOe; therefore, they concluded that there was no change in the excitation threshold of nerve exposed to fields of this intensity. Selivanova (8), on the other hand, noted a reduction in spinal reflex time in frogs exposed to magnetic fields if the spinal cord was sectioned to produce measurable inhibition. He concluded that a constant magnetic field reduced inhibition and caused a time reduction in functional measurements. The wide divergence of conclusions based on these results is evident. One objective of our experiments was to resolve these apparent contradictions.

Many of those investigators stressed the difficulties involved in developing a unified theory that would explain the observed effects on a biophysical or physicochemical basis. A second, and equally important, aim of this study was to approach the understanding necessary to develop such a theory.

Considerable insight into the physiological state of a functional nerve may be gained from measurements of the rate of impulse propagation. Dynamic measurement of changes in this state, due to a physical force such as a magnetic field, requires that those measurements be taken coincidentally with the field in both time and space. Another important consideration is the well-known dependence on orientation of the physical interactions between a magnetic field and electrical charges in motion. This study was designed to take into account all of these factors.

PROCEDURE

MATERIAL

Preparations of the sciatic-peroneal nerve were obtained by dissection from Rana pipiens. Considerable care was taken to prevent desiccation and stretching of the nerve either before or during transfer to the recording chamber. The nerve trunk was

ligated with 6-0 silk sutures at the cut ends and these sutures used to guide it into the chamber containing paraffin oil. Minimum distance between the ends of the nerve and any of the electrodes was 8 mm.

CHAMBER

The recording chamber was constructed from plastic with one section at 90° to the other. The inner dimensions were chosen so that both sections were located within a field volume well inside the edges of the pole caps (Figure 1). This arrangement minimized the field gradient affecting the nerve. Outer dimensions equal to the pole gap and an indexed support rod guided the chamber into the same relative position in the field at each trial.

Pairs of platinum stimulating and recording electrodes were spaced to provide an interelectrode distance of 5 mm. One pair of recording electrodes was located in each leg of the L-shaped chamber. Each pair was positioned so that an impulse arriving at the more proximal electrode of the pair had previously traversed a 5-mm section of the nerve oriented either parallel or perpendicular to the field. The stimulating electrodes were 30 mm from the nearest recording electrode to minimize stimulus and electrotonic artifacts.

STIMULUS

A square pulse of 18 μsec duration was applied at a frequency of 50 Hz to trigger the nerve and the oscilloscope.

FIELD MEASUREMENTS

The magnetic field was generated by a conventional, dc, water-cooled electromagnet energized by a power supply which had a stability of 1 part in 10^5 (Harvey-Wells Corp., Framingham, Mass.). Determinations of the intensity and polarity of the field were made by a gaussmeter based upon the Hall effect (Model 620, F. W. Bell, Inc., Columbus, Ohio) with a high-accuracy, temperature-compensated probe (Model T-6030). Resolution was increased by the readout from a digital voltmeter (Model 6653, Cimron Div., Lear Siegler, Inc., San Diego, Calif.) connected to the gaussmeter. The probe was positioned in the field by a rigid nonmagnetic mount that provided movement in three axes in indexed increments of 1 mm. After correction for nonlinearity in the Hall element, it was found that the maximum field over the entire length of nerve varied between 11.701 and 11.641 kOe. The average field affecting the nerve was 11.671 kOe. The field gradient over the segment of nerve perpendicular to the field was calculated as 11.1 Oe/cm by dividing the maximum difference in field along that segment by its length. A gradient of 18.8 Oe/cm along the nerve parallel to the field was computed in the same manner. Polarity of the magnet was such that the perpendicular segment of nerve was proximal to the North magnetic pole, with the parallel segment extending along the Z-axis toward the South pole (Figure 1).

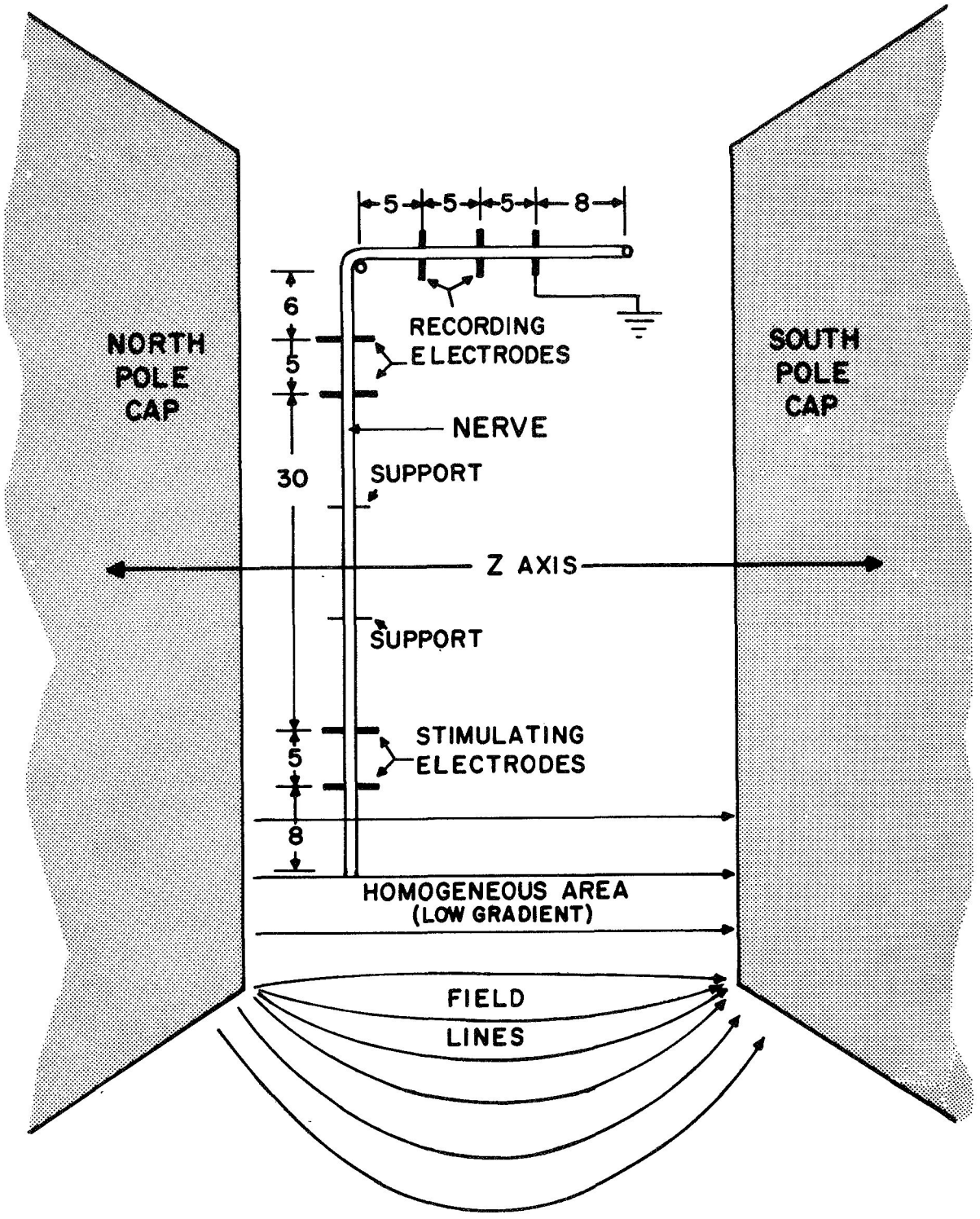

Figure 1

Position of the nerve and electrodes in the magnetic field. Interelectrode distances are indicated in millimeters and are to scale. The field is radially symmetrical about the Z axis. The chamber was designed so that both the parallel and perpendicular segments of the nerve were in the homogeneous or low-gradient area of the field.

METHOD

Signals from each of the four recording electrodes were carried on individually shielded leads to the preamplifiers of a four-channel oscilloscope (Tektronix Type 565). By this method it was possible to terminate the shield at the input of the amplifier processing the signal from each electrode. A double-walled, grounded enclosure around the nerve chamber provided no further improvement in the signal-to-noise ratio. The two displays from each pair of electrodes were referenced to the same time base within the oscilloscope.

Polaroid photographs of the four-trace display were taken at selected time intervals by an oscilloscope camera. Peak-to-peak measurements of the time interval between biphasic action potentials registered at each electrode of a pair provided the data required to calculate conduction velocity by the formula

$$\bar{v} = \frac{s}{t}$$

where $\bar{v}$ = the mean velocity of the individual fibers,
s = the distance between the electrodes of a pair,
t = difference in the time required for the potential to appear at those electrodes.

A grid was projected onto the oscilloscope face so that both grid and display were in the same plane. A second overlay grid was prepared by a 4:1 photographic reduction of the grid used for projection. A further increase in resolution was obtained by superimposition of this overlay upon the photographs and subsequent examination with a dissecting microscope. Accurate measurements of increments in time of 15 μsec were possible by this method. Errors in time measurements from which the conduction velocity was calculated and the consequent error in velocity were thus reduced to only 2 to 5 per cent at normal rates of propagation. As in all calculations of velocity, the effect of a constant error in time measurement increases as the increments of time decrease. The error in the highest velocities reported here may, therefore, reach 10 per cent.

No specific effort was made to differentiate between the effects of the field on α and β fibers; however, peak-to-peak measurements of this type tend to accentuate the contribution of the α fibers due to their lower threshold, higher conduction velocity, and greater number.

Controls

An experimental sequence consisted of three parts: a preexposure control period before the magnet was energized, the period of exposure to the magnetic field, and a postexposure control period after the magnet was switched off. Each nerve, therefore, served as its own control.

Several additional experiments were conducted to detect and minimize artifacts. Induced electrical artifacts would be coincidental with and directly dependent upon the presence of the field. A slave oscilloscope and a tape recorder monitored the nerve output during switching of the magnet in the preliminary and early experimental trials. There was no evidence of switching transients on the oscilloscope, on replay of the tape at increased gain, or in any of the experimental records.

Several preliminary experiments were conducted to establish the normal changes to be expected with time in nerve under in vitro conditions of this nature. In two of these preliminary trials conditions were identical to those of the experimental series with the exception that the magnet was not energized. Deterioration with time in these preparations was expressed as a gradual decrease in amplitude of the action potential and as a decrease in conduction velocity.

Another artifact to be considered was the possible effect of a change in temperature within the chamber due to heat dissipated from the coils of the magnet. An additional control experiment was conducted to evaluate this possibility. A thermister was substituted for the nerve in the oil-filled chamber, and the magnet operated at full power for a time period equal to that in the experiments. The maximum temperature fluctuation was less than 0.3°C.

Data Analysis

Three factors in addition to the magnetic field operate concurrently to influence the absolute velocity values obtained in these experiments: The wide variation in the conduction velocity of individual fibers of compound nerves is well known, as is the fact that this velocity is constant (9). The generally accepted range in values of velocity for frog sciatic nerve is from 0.3 to 42.0 m/sec. Similar differences in velocity between different preparations were noted in our experiments during the preexposure control periods. The errors in time measurement and changes due to deterioration described earlier also influence the velocity determinations.

Since those factors affect the results of individual experiments in differing degrees, a direct comparison of conduction velocities is difficult. Our method of data analysis was adopted to overcome this difficulty.

RESULTS AND DISCUSSION

Figure 2 indicates the results of a representative experiment in terms of the absolute conduction velocities calculated from measurements of the experimental records. This figure, therefore, indicates typical, original data as obtained during each of the individual experiments.

Figure 3 shows the relationships between the absolute velocities obtained in the individual experiments normalized to a common preexposure baseline. This baseline was calculated for each experiment as the mean of five preexposure velocity measurements. All baselines were arbitrarily established at 100 per cent to indicate the

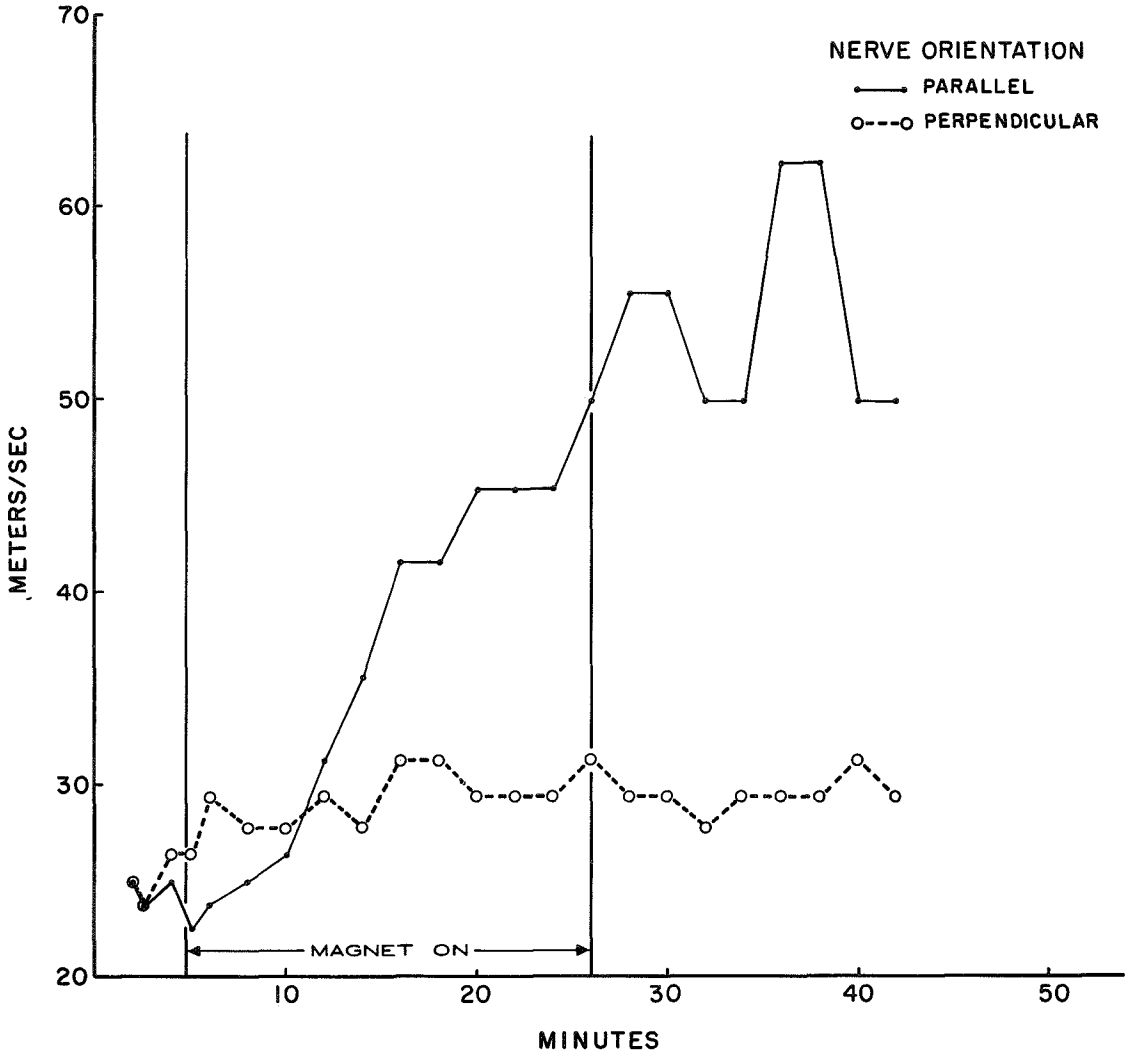

Figure 2

Effects of orientation on conduction velocity in sciatic nerve exposed to a magnetic field of 11.6 kilo-oersted.

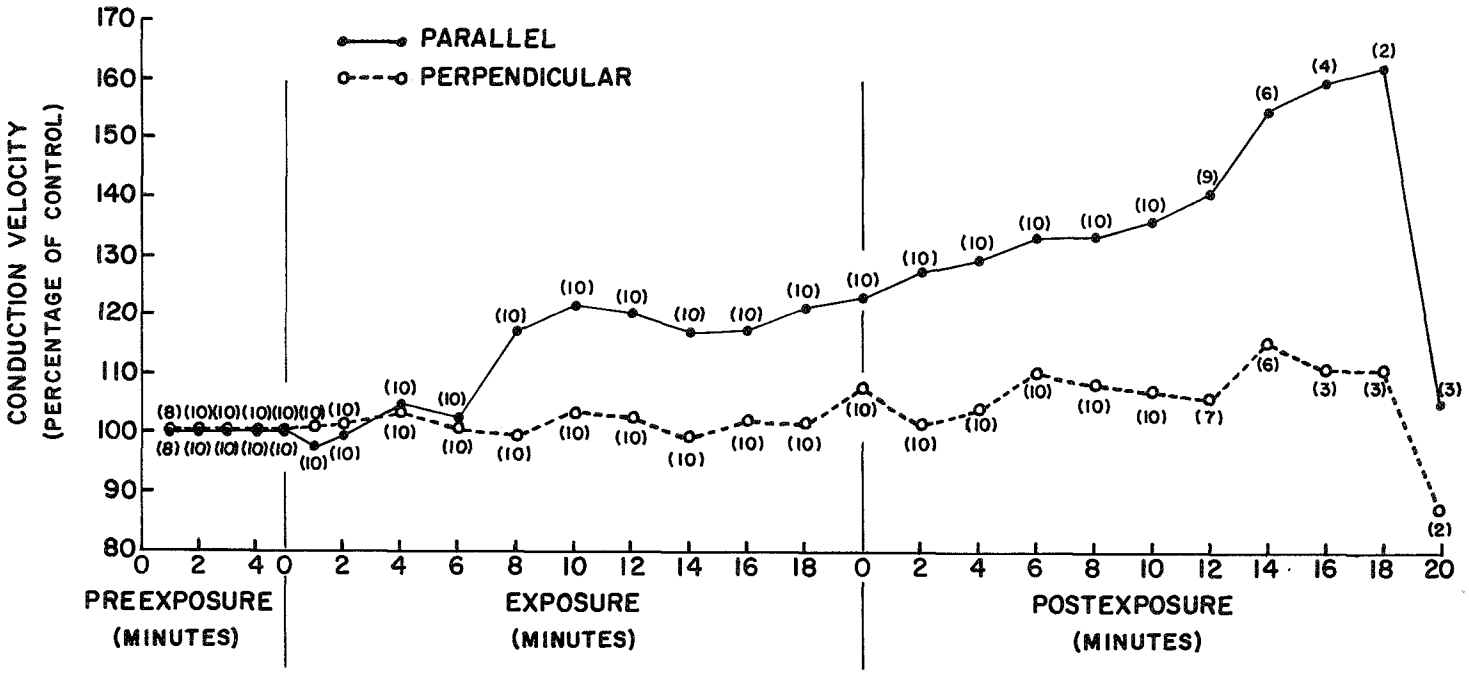

Figure 3

Changes in conduction velocity in nerves oriented parallel and perpendicular to a magnetic field of 11.6 kilo-oersted. Parenthetical numbers above and below the curves indicate the number of experiments contributing data to establish that point. See text for procedure used to normalize results of individual experiments.

condition of the nerve prior to exposure to the magnet. Conduction velocity was determined at 2-minute intervals thereafter and expressed as a percentage of the base-line. The mean of these percentages for all experiments then represented the mean deviation from the preexposure baseline at each 2-minute time increment.

The studies presented here indicate that high magnetic fields can cause detectable changes in the physiological state of isolated nerves. They differ in two significant aspects from similar studies previously reported. Both of these differences emphasize the need for a dynamic approach to investigations of this type; either could account for the apparently contradictory results of earlier work.

The first major difference takes into account the fundamental ability of a nerve fiber to resume normal conduction characteristics once the impulse has traversed an injured or affected area. This ability is related to the well-known "all-or-nothing" and local circuit properties of functional nerve. Tasaki (10) provided an example of this in his description of very early work by Adrian. Adrian demonstrated that an action potential which had been reduced in amplitude in passing through an anaesthetized zone on the nerve recovered its normal properties once it reached an unanaesthetized area. Given this property of nerve, it follows that the best measurement of a change should be obtained from within the affected area. This was a part of the rationale in our experiments but apparently was not that in the earlier investigations where the recording electrodes were located outside this area. As mentioned earlier, nervous system changes have been found in whole animals exposed to high magnetic fields. It is of interest to note that most of the measurements of these changes were obtained from a point within the magnetic field.

The second significant difference between our studies and those reported earlier lies in the stress placed upon the vector characteristics of a magnetic field. Our experiments were designed to detect the effect of changes in the relationship of this vector to the nerve by changing the orientation of the nerve to the field. The earlier investigations involved a single, perpendicular orientation of the field and, consequently, a single vector. The consistent results of the studies on the entire animal may also be explained on this basis if one considers the numerous orientations of the nervous system to an imposed magnetic field. Under these conditions the influence of the magnetic vector must be very different at different parts of the system.

Even a cursory examination of Figures 2 and 3 indicates that high magnetic fields cause changes in nerve which are reflected as an increase in conduction velocity. It is equally evident that the magnitude of these changes is directly dependent upon the orientation of the nerve relative to the field.

For the sake of clarity, however, this part of a more detailed analysis of the results is limited to a discussion of the curve depicting the response of the nerves parallel to the field (upper curve, Figure 3) and will disregard orientation. A displacement in time was noted in that the beginning of the increase in velocity was not coincident with the field. There was a definite delay, or latent period, between the

beginning of exposure to the field and the changes in velocity. This latent period appears to be characteristic of the interaction of magnetic fields with neural elements since it has been observed previously (11).

Following the latent period there was a sudden increase in velocity that stabilized to a state in which the acceleration in rate was constant until 12 minutes after exposure. This suggests that the nerves passed through an unstable stage preceding a period of readjustment; the resultant of this readjustment was a constant increase in velocity. The reliability of the data taken after 12 minutes postexposure is not high because of the limited number of measurements. The data do indicate, however, the beginning of another perturbation of the conditions prevalent at that time. The sudden decrease in velocity 18 minutes after exposure is probably not a magnetic effect but is more likely due to the cumulative effects on the nerve of fatigue, lack of nutrients, and hypoxia.

The implications of the postexposure increase in velocity may be quite meaningful, and this point merits further investigation. There is no evidence in this study of a recovery of normal functions after the magnet was switched off. This may indicate either a permanent change in the nerve or that the time span of the experiments was insufficient to permit recovery to take place. The persistence of the aftereffect seems to be another characteristic magnetic effect and has also been observed in other studies (1, 11-13). Young and Gofman (13) pointed out that this aftereffect lasted for at least 2 hours but had disappeared by 18 hours. It seems likely, therefore, that our experiments were too brief in duration to observe a return to normal velocities.

Probably the most significant result of our study, from the theoretical point of view, is that the magnitude of the increase in conduction velocity is a function of the orientation of the nerve to the field. Both the duration of the latent period and the rate of change in velocity are orientation dependent (both curves, Figure 3). This is strong evidence tending to confirm the original hypothesis that magnetic effects should be dependent on orientation because of the vector nature of a magnetic field. It also demonstrates that with proper experimental design, magnetic effects can be explained on a physical, rather than an empirical, basis.

The latent period was much greater in duration, and the increase in velocity considerably reduced in amplitude, in the nerve perpendicular to the field (Figure 3). The degree and direction of these changes suggest the existence of a threshold below which no effect would be detected in nerve having this orientation. It appears that this threshold was barely exceeded under the conditions of our experiments. Insofar as it can be determined, previous *in vitro* studies (5-8) were conducted exclusively upon nerves oriented perpendicular to the field. The minimal changes obtained under these conditions may account for some of the contradictions in the earlier work.

Since only one facet of impulse propagation was investigated in this study, definite conclusions concerning mechanisms of action are not justified. It may be useful, however, to point out possible mechanisms that should be considered in future experimentation. At least three properties of the nerve and one of the field may act

either singly or in concert to produce the observed effects: 1) Transmembrane movement of sodium and potassium may be altered. 2) Membrane permeability may be affected by structural rearrangement. 3) Hall voltages generated across the membrane could polarize the nerve. 4) Field inhomogeneities could affect nerve constituents according to their magnetic properties.

The symmetry of the nerve relative to the field lines should be borne in mind as these possibilities are considered in more detail. If there are no differences in gradient along either the longitudinal or transverse axes of the nerve, forces exerted by a magnetic field would be applied in a radially symmetric configuration to a nerve oriented parallel to the field, but would be asymmetrically disposed across the diameter of a nerve located at any other angle.

It is well known that the force exerted upon a charged particle moving through a magnetic field is at a maximum if the direction of this movement is perpendicular to the field. This condition prevails at every point in the membrane of the nerve fiber parallel to the field where the direction of movement of sodium and potassium ions is perpendicular to the field; therefore, they should experience a maximum force. This is not the case if the nerve is perpendicular to the field where the greater percentage of ion movement is either at 0° or at an angle less than 90°. A differential effect of the field related to its orientation to the nerve would be expected on this basis; however, there is a further difficulty. If the forces acting to deviate the ions from their normal path through the membrane are at a maximum in the nerve parallel to the field, one would expect a decrease in the rate of ion movement and in the forward velocity of an impulse, due to increased resistance between the ions and the walls of the membrane "channel." This decrease would be directly related to the angle between the direction of ion movement and the field. The results of this series of experiments, however, indicate a response to the field opposite in direction to that predicted by this hypothesis; i.e., an increase in velocity directly related to this angle.

Another credible hypothesis is that the magnetic field affects the permeability or structure of the membrane itself rather than the ions moving across that membrane. Bachofer (14) has proposed such a mechanism to account for an increase in conduction velocity observed in nerve exposed to ionizing radiation.

If one accepts the increasing evidence that intracellular sodium and potassium ions in the nerve obey laws analogous to those pertaining to the conduction of electrons in semiconductors, yet another mechanism is suggested. Hall voltages generated across the nerve during the passage of an impulse could affect either the movement of ions through the membrane or the nerve threshold by partial depolarization. Becker has, in fact, reported the presence of Hall voltages in salamanders exposed to magnetic fields (15) and Beischer (16) noted potentials entirely analogous to Hall voltages in the VCG of monkeys in a superconductive magnet.

Practical considerations in magnet design make it very difficult to equate the field gradients affecting all parts of a specimen oriented as in our experiments. Even

though the gradient differences obtained were small, possible differential effects of the field on para- and diamagnetic components of the nerve cannot be eliminated as a factor capable of producing the observed changes.

None of these hypothetical mechanisms of action of a magnetic field can be rejected on the basis of information available to date; a more complete understanding of the interaction of neural elements with a magnetic environment can be approached only by further experimentation. The studies on conduction velocity presented here demonstrate that this interaction produces measurable changes of physiological significance and emphasize the need for this experimentation.

REFERENCES

1. Beischer, D. E., and Knepton, J. C., Jr., Influence of strong magnetic fields on the electrocardiogram of squirrel monkeys (Saimiri sciureus). NSAM-888. NASA Order No. R-39. Pensacola, Fla.: Naval Aerospace Medical Institute, 1964.

2. Beischer, D. E., and Knepton, J. C., Jr., The electroencephalogram of the squirrel monkey (Saimiri sciureus) in a very high magnetic field. NAMI-972. NASA Order No. R-39. Pensacola, Fla.: Naval Aerospace Medical Institute, 1964.

3. Mutschall, V., Biological effects of magnetic fields. Foreign Sci. Bull., 5:13-36, 1969.

4. Kholadov, Yu. A., The effect of electromagnetic and magnetic fields on the central nervous system. NASA TT F-465. Washington, D. C.: National Aeronautics and Space Administration, June 1967.

5. McKendrick, M., Observations on the influence of an electromagnet on some of the phenomena of a nerve. J. Anat., 13:219-223, 1879.

6. Drinker, C. K., and Thomson, R. M., Does the magnetic field constitute an industrial hazard? J. Ind. Hyg., 3:117-129, 1921.

7. Liberman, E. A., Vaintsveg, M. N., and Tsofina, L. M., The effect of a constant magnetic field on the excitation threshold of isolated frog nerve. Biofiz., 4:505-506, 1959.

8. Selivanova, E. V., Effect of a steady magnetic field on the phenomenon of Sechenov's inhibition. Biofiz., 1:412-415, 1956.

9. Erlanger, J., and Gasser, H. S., Some reactions of nerve fibers to electrical stimulation. In: Electrical Signs of Nervous Activity. Philadelphia, Penna.: Univ. of Pennsylvania Press, 1937. Chapt. 3, p. 79.

10. Tasaki, I., The "all-or-none" law. In: Nerve Excitation. Springfield, Ill.: Charles C Thomas, 1968. Pp 8-10.

11. Reno, V. R., and Beischer, D. E., Cardiac excitability in high magnetic fields. Aerospace Med., 37:1229-1232, 1966.

12. Chalazonitis, N., and Arvanitaki, A., Effets du champ magnétique constant sur l'autoactivité des fibres myocardiques d'Helix pomatia. C. R. Soc. Biol. (Paris), 158:1902-1908, 1964.

13. Young, W., and Gofman, J. W., Magnetic fields, vagal inhibition, and acetylcholinesterase activity. Report UCRL-12389. Livermore, Calif.: Lawrence Radiation Laboratory, Feb. 1965.

14. Bachofer, C. S., Enhancement of activity of nerves by x-rays. Science, 125: 1140-1141, 1957.

15. Becker, R. O., Search for evidence of axial current flow in peripheral nerves of salamander. Science, 134:101-102, 1961.

16. Beischer, D. E., Vectorcardiogram and aortic blood flow of squirrel monkeys (Saimiri sciureus) in a strong superconductive electromagnet. NAMI-1036. NASA Order No. R-39. Pensacola, Fla.: Naval Aerospace Medical Institute, 1968.

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13. ABSTRACT

Action potentials were recorded at four positions from frog sciatic nerves exposed to a constant magnetic field of 11.6 kilo-oersted. External electrodes arranged in pairs on segments of nerve oriented both parallel and perpendicular to the field permitted conduction velocity measurements to be expressed as a function of field orientation. An increase in conduction velocity was observed to be orientation dependent as was a latent period in its appearance. An aftereffect was noted that persisted to the end of the experiments. Possible mechanisms of action of the field are discussed in terms of current theories of impulse propagation.

14. KEY WORDS	LINK A		LINK B		LINK C	
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Nerve						
Orientation						
Conduction velocity						
Latency						
Magnetic vector						