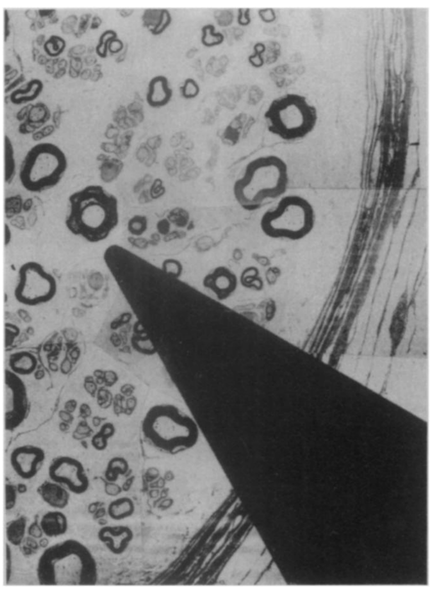
Wiretap on the Nervous System

Scientists are listening in on the signals going to and from the brain



Ochoa

Electrode picks up signals from individual fibers, 1 to 15 microns in diameter, within a nerve (shown in cross section).

By JULIE ANN MILLER

Eavesdropping on the human nervous system, and even whispering commands to it, is now possible with an electrical recording and stimulating technique. With a fine metal electrode inserted into the arm or leg of an awake volunteer, scientists are learning what nerve fibers are involved in a variety of sensations, movements and subconscious activity. And they are beginning to investigate what goes wrong in specific diseases.

"You can't study voluntary, high-level movements in deeply anesthetized cats. And you can't go prowling around in a human brain," says Robert R. Young of Massachusetts General Hospital and Harvard Medical School in Boston. "But there is a lot of basic scientific data to be obtained from human beings who can tell you what they are feeling and doing."

The technique, originally developed 15 years ago in Sweden, is now used by about 30 research groups around the world. The recently formed International Microneurography Society, which Young heads, has 60 members.

"More and more people are using this technique, although it is very time-consuming," Young says. "It requires a certain kind of person [researcher], with skillful fingers and a lot of patience." And it requires patient subjects who will lie still for a couple of hours without twitching or sneezing.

At the recent meeting in Minneapolis of the Society for Neuroscience, Young was chairman of a symposium entitled Physiological Insights Derived from Nerve Traffic Analysis in Conscious Man. The program brought together people using the technique to examine diverse questions — from mapping pain and itch to exploring nervous sweat. And it presented to scientists working primarily on animal nervous systems what can be learned with this technique about human beings.

In the experiments an electrode is stuck into the arm or leg of a resting volunteer. The electrode is angled, like a lead pencil, to a point a few microns across. It is so sharp that insertion is not painful, the investigators say. It takes about half an hour to locate the needle correctly.

The electrode is inserted into a nerve, which contains bundles or fascicles of fibers coming from individual nerve cells. Each fascicle contains functionally related nerve fibers, such as those carrying signals to muscle or those bringing information from sensory organs at the skin. The investigator positions the electrode next to a fiber, which can be 1 to 15 microns in diameter. "It's like spearing eels in a bathtub," Young says. The electrode then reports each nerve impulse that passes along the fiber.

Finding out the role of individual nerve fibers in sensing touch is the goal of the work reported by Åke Vallbo of the University of Umeå in Sweden. He positions the electrode next to a nerve fiber in the subject's arm and then determines what sensation on the subject's hand will make the fiber respond. Some fibers respond to a touch, rub or pinch; others react to heat or cold. The characteristics of the response also vary. A fiber may fire only a few times, fire continuously or fire only when the sensation starts and stops. The fibers have been categorized by these characteristics.

Vallbo has determined the roles of four types of skin sensory units having relatively thick nerve fibers. Two (called RA and SA I) are involved in spatial analysis of tactile stimulation. For example, even in the dark a person can hold onto a small object, like a die. Sensory inputs traveling along these types of nerve fibers are processed in the brain to tell the finger muscles to adjust the grasp appropriately. Some of these signals cause no conscious sensation.

Other fibers seem to carry information about the location of a person's limbs and whether the joints are flexed or extended. These signals travel along the nerve fibers designated PC and SA II, Vallbo suggests. Some of this information comes from sense organs that detect how tight the skin is stretched. The electrical signals of these fibers are closely related to movement and position, Vallbo reports.

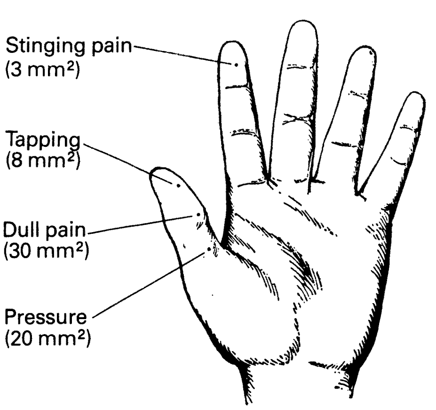
Turning around the original use of the electrodes as recording tools, Erik Torebjörk of University Hospital in Uppsala, Sweden, commands the nerve fibers rather than just eavesdropping on them. In work with Jose Ochoa of Dartmouth Medical School, he positions the needle next to a fiber and gives pulses of current. Then the subject reports on the resulting feelings. "The brain can discriminate quality, magnitude and temporal profile from a single sensory input," Torebjörk says.

What the subject feels from stimulation of one of certain nerve fibers in the arm, is touch or pressure or pain or itch at a specific point on the hand. Some fibers respond to a single pulse, others need a series. In some cases the subject reports no sensation at all.

"The brain has an extraordinary capacity to sense from a single nerve cell in the hand, even a single impulse," Torebjörk says. He thinks it unlikely that sensation from other areas of the skin is so acute. He has learned that within a fascicle, nerve fibers are not organized according to location or quality. When an electrical impulse that causes a sensation of intermittent tapping is increased in intensity, so it activates a neighboring fiber, the subject reports a second, separate sensation — for example, pressure some distance away from the location of the tapping sensation. Most nerve fibers going to a given finger are together in one fascicle, however. Torebjörk finds in his stimulation experiments correlations consistent with the data from the work recording nerve fiber activity.

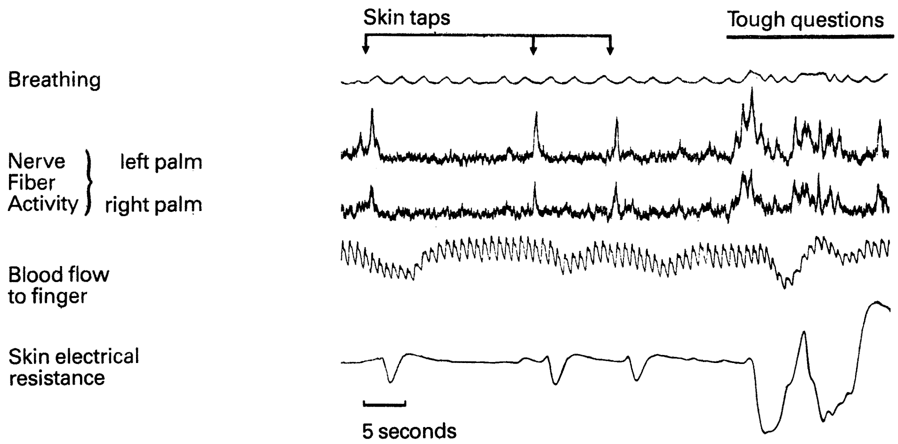
The action of the nerve network responsible for control of some other body functions is more complex than scientists had thought, according to the work of B. Gunnar Wallin of University Hospital in Uppsala, Sweden. He studies the nerve fibers carrying signals from the brain to blood vessels and sweat glands, in order to regulate body temperature, blood pressure, sweating and such skin color changes as blushing. These nerves are part of the sympathetic nervous system. "You ordinarily don't feel much of this regulation," Wallin says. But these functions react dramatically to emotion.

"With this new technique all of a sudden it becomes possible to record nervous system activity in man, unanesthetized. The subjects can tell what he feels, so you know his emotions," Wallin says. It becomes "possible to get direct information about sympathetic neural outflow to skin and muscle, not only at rest and during various external maneuvers but also during emotional and mental reactions which are difficult or impossible to study in animals."



Subjects report specific, localized sensations in response to pulses of current applied to nerve fibers.

A Cold Sweat Diagrammed



Nerve fiber activity underlies breathing, blood flow and skin responses to disturbances of a subject lying at rest. Adapted from Lidberg, Wallin/Psychophysiology, ©1981 The Soc. for Psychophysiological Res.

In a sense, this use of the technique can be considered an exceptionally sensitive lie detector test. Instead of recording electrical resistance, which reflects sweating of the skin, Wallin records the nerve signals that direct the sweat glands. His work can reveal the detailed physiology underlying a widely used but empirically developed forensic tool.

Microneurography applied to the sympathetic nervous system has changed a basic concept of physiology. Scientists had thought that the sympathetic nervous system reacts as a whole to stimuli, setting a single tone for all its parts. But Wallin has demonstrated differentiated control for the various targets.

In a typical experiment the subject is lying, eyes closed, in a silent room. Wallin monitors the activity of fibers innervating either the foot or palm of the hand. He can record two types of impulses, each in a different nerve fiber, going to the skin. The slower impulses control blood vessel constriction; the faster stimulate the sweat glands.

When a subject at rest suddenly feels a touch or hears an unexpected sound, Wallin records a single burst of impulses in both types of nerve fibers going to the skin. If the subject is then asked "a little bit nasty question" there is much long-lasting nerve activity in fibers going to the skin. In contrast, an increase in room temperature has opposite effects on the fibers — it increases sweating but decreases constriction of blood vessels.

Wallin has also examined nerve fibers going to muscle. He observes bursts of activity primarily during transient reductions in blood pressure. These nerve signals seem to be important for buffering moment-to-moment changes in blood pressure. Without such control, the blood pressure of a person who goes from lying to standing would drop and the person would faint. (In fact, Wallin has recorded from a subject who happened to faint during the experiment. Activity disappeared along the nerve fibers going to muscle, then gradually the activity resumed.)

Simultaneous recordings from a fiber going to skin and one going to muscle show the impulses occur independently and the responses to various situations differ. The nerve fibers going to muscle do not generally respond to arousal stimuli, such as nasty questions, unless blood pressure is also affected.

"The findings show that sympathetic outflows to different regions are controlled differentially," Wallin says, "and consequently the old view of a diffuse sympathetic tone that fluctuates in parallel in different organs cannot be maintained." Wallin suggests the technique is well-suited to investigate certain diseases, such as hypertension, and also to study the actions of drugs.

Understanding of how voluntary movements begin also has changed dramatically in response to studies of individual nerve fibers. The idea that had held sway from 1945, called the servomechanism theory, was modeled after the way large cannons were moved during World War II. Soldiers used a mini-cannon that could be easily moved, a sensing device and a motor instructed to minimize the difference in orientation between the mini-cannon and the true weapon.

In the theory of muscle movement, the mini-cannon is the muscle spindle — a sense organ responsive to the muscle's stretch. The spindle is itself a cluster of small muscles enclosed by a capsule. Muscle spindles send signals triggering the reflexes that continually and subconsciously adjust muscle contraction, for instance to keep a person from falling when walking. "Spindle activity makes motor performance smooth, damping jerkiness," Karl-Erik Hagbarth says. "It is of great importance for voluntary motor control."

According to the servomechanism idea, movement begins with a signal to the

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muscle spindle, which in turn sends a signal to the brain to adjust the muscle to match the spindle. But recording activity of the nerve fibers going to muscle spindles has shown that this theory is incorrect.

"Our first goal was to study incoming signals from muscle spindles," says Hagbarth, of University Hospital in Uppsala. He and Vallbo together started the microelectrode recording technique using themselves as subjects. They discovered that movement is initiated not by a servomechanism, but more directly by a nerve impulse traveling from the brain to the spinal cord and then to the muscles. Scientists now agree that the nerve fibers going to the muscle spindle, on the other hand, keep the organ adjusted to an appropriate length to continue to sense muscle length changes. Otherwise when the muscle shortens, for example, the spindle would go slack and no longer be useful to sense muscle length.

Clinical research on patients with neurological disorders is just beginning. Hagbarth and Young have studied subjects with different types of tremors. Trembling is the result of spindle activity making muscle fibers contract in groups, rather than at different times. This results in a hand, for instance, jerking up and down instead of remaining steady.

Parkinson's disease and the hereditary condition called benign essential tremor involve the muscle spindles only indirectly, the investigators find. The problem in these cases occurs in the brain or spinal cord. But nervous tremor, the stage fright everyone experiences from time to time, does originate at the spindle. So does trembling from caffeine, low blood sugar and some asthma drugs.

Young explains that adrenaline, released as part of the body's "flight-or-fight" response, changes the mechanical properties of muscle, making it contract more strongly and quickly and become more resistant to fatigue. As a side effect, the spindles are stimulated sooner and more often. Consequently they make groups of nerve cells going to muscle fire more synchronously. "These bursts are good for a quick jump or fast run," Young says. "But it is embarrassing and can be disabling to a musician, marksman or surgeon." Young says that many such professionals now take a drug, propanolol, that blocks adrenaline's action on muscle.

From pinches to tremors, a few secrets of the nervous system have already been detected by the eavesdropping scientists. But they believe the greatest discoveries of the technique are soon to come. With a combination of stimulating and recording from single nerve fibers while observing what the subject feels and does, they hope to understand subtle aspects of perception and reaction at a higher level than is possible from studying animals. □

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Annual Review of Psychology, Vol 34 — Mark R. Rosenzweig and Lyman W. Porter, Eds. The prefatory chapter for this volume is "Behavioral Medicine: Symbiosis Between Laboratory and Clinic" by Neal E. Miller, Rockefeller University. Annual Reviews, 1983, 623 p., $27.

The Atlas of Archaeology — K. Branigan, Ed. Presents a unique dual chronicle of past civilizations and of archaeology as a science. Focuses on the discoveries at 50 significant sites throughout the world. Each site is treated in two double-page spreads: the first describes how the site was excavated and its major finds, the second, illustrated by artwork reconstructions, describes the way of life of the people, their architecture and artifacts. St Martin, 1983, 240 p., color/b&w illus., $25.

Gardening with Native Plants of the Pacific Northwest — Arthur R. Kruckeberg. In the Pacific Northwest is a great diversity of climate, terrain and natural vegetation. The vegetation includes a rich variety of native plants of ornamental value to enhance the gardens and urban landscapes of the region. This book identifies these plants and describes their natural habitats and methods of propagation and cultivation. U of Wash Pr, 1982, 252 p., illus., $24.95.

Maximum Life Span — Roy L. Walford. Presents the history and future of gerontological research and describes how we can begin preparing for the changes that will occur in our society with the advent of an extended life span. Explains various theories of aging, the aging process itself and tells how individuals can improve their own survival chances. Norton, 1983, 256 p., charts & graphs, $15.50.

New Plant Sources for Drugs and Foods from The New York Botanical Garden Herbarium — Siri von Reis and Frank J. Lipp, Jr. Presents data relating to unusual drug and food plants culled from the N.Y. Botanical Garden Herbarium. The authors express hope that these potentially useful species will be studied and evaluated before their natural environments are disturbed and the plants become extinct. Harvard U Pr, 1982, 363 p., $25.

The Politics of Reproductive Ritual — Karen Ericksen Paige and Jeffery M. Paige. Most societies have some behavioral restrictions or emotionally charged beliefs about the major events of the human reproductive cycle. Even in contemporary industrial societies menstruating women, according to the introduction, are widely regarded as irritable and emotionally unstable. This book presents a theory to explain the nature and distribution of reproductive rituals in preindustrial societies and provides a starting point for analysis of beliefs about women and reproduction in industrial societies. Originally published in hardback in 1981. U of Cal Pr, 1983, 380 p., chart & graphs, paper, $8.95.

The Youngest Science: Notes of A Medicine-Watcher — Lewis Thomas. A personal memoir, combining this outstanding physician's meditations on medicine and biology with an account of his own medical career. Recollections of his father's medical practice in the 1920s through Thomas's own medical education and career make this a fascinating account of the development of modern medicine. Viking Pr, 1983, 270 p., $14.75.

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