Neuron selectivity: Down memory lane

Researchers have recorded the activity of single neurons within the medial temporal lobe — a brain region important in memory formation — and found the first evidence in humans that individual nerve cells apparently recognize specific words and are important in short-term memory.

Eric Halgren of the University of California at Los Angeles and his colleagues took advantage of electrodes temporarily implanted in the brains of 10 patients undergoing neurosurgery for epilepsy. They asked patients to memorize 20 abstract words shown on a video monitor, then gave them recognition tests and recorded their neuronal responses.

Most neurons tested, the team found, displayed a preference for specific words. For instance, one cell fired repeatedly at "luck," another at "woe."

"A striking feature of these data," notes Michael Rugg of the University of St. Andrews, Fife, Scotland, in a commentary accompanying the report in the June 23 NATURE, "is the frequency with which word-specific responses were observed." In 75 percent of neurons tested, the nerve cells preferred one or more of the words listed. This high rate with the small number of cells tested does not mean that each cell memorizes just one word. Instead, say the researchers, it means that a word evokes activity in many neurons, only a few of which were tested.

The group had set out to learn how damage to the medial temporal lobe causes a peculiar inability to recall words and faces seen very recently, while the ability to use language remains. The findings support the view that structures within the medial temporal lobe help a person remember the context in which a complex stimulus, such as a word or face, was encountered — but not those aspects of the stimulus that remain constant, such as meaning or pronunciation. The researchers say their data suggest the medial temporal lobe "contributes specific information rather than diffuse modulation to the encoding and subsequent recognition of a stimulus during recent memory." In other words, says team member Gary Heit, "it's like shining a flashlight on one picture rather than turning on all the lights in the room."

Other implications of the work are open to interpretation. Contrary to what might have been expected, the researchers found a neuron's response to a word *un*affected by repetition: Whether the word "luck" was shown once or 10 times, neuronal firing remained the same. Rugg questions the authors' explanation that repetition does not affect the output of information from this area to other brain regions. — *C. Eron*

Hairy portals for toxic chemicals

Toxicologists tend to focus on the nose and mouth as passageways through which hazardous chemicals enter the body. Skin is another portal for these chemicals, but its role is far less understood. Conventional wisdom has held that the skin's outermost layer of dead cells served as a passive barrier, and that simple diffusion set the rate at which chemicals passed through this inert filter. But that didn't explain why skin permeability at different parts of the body can vary dramatically. A study performed at Oak Ridge (Tenn.) National Laboratory now reveals that structural factors in skin — like hairiness — can affect absorption.

Skin does not present a uniform barrier. Among the "holes" penetrating it are hair follicles, sebaceous glands and sweat glands. John Kao (now at Smith Kline and French Laboratories in King of Prussia, Pa.) and his co-workers at Oak Ridge decided to examine the role of such holes by measuring the penetration of two chemicals — the male hormone testosterone and the pollutant benzo[a]pyrene (BP), a suspected human carcinogen — in skin cultured from hairy and hairless strains of mice.

Their findings, reported in the June 15 TOXICOLOGY AND APPLIED PHARMACOLOGY, show that 4.4 to 9.4 percent of the BP penetrated the skin from hairy mice — two to three times more than was absorbed through the hairless-mouse skin. Testosterone, however, penetrated both types of mouse skin equally — about 12 to 16 times more readily than BP passed through hairy-mouse skin.

The reason for the chemical differential, explains Jerry Hall, one of the study's authors, is metabolism. The researchers had previously found that healthy skin, far from being inert, can conduct "extensive" metabolism — or biological alteration — of chemicals. And this can affect a chemical's skin-penetrating ability.

As fat-seeking chemicals, both BP and testosterone will preferentially deposit at the hair follicles and sebaceous glands, focal sites of metabolic activity. BP must be altered by an enzyme in order to penetrate. Testosterone, however, can pass through directly. It now appears, Hall says, that hair follicles and glands can play a major role in chemical absorption through the skin, especially with those fat-seeking chemicals like BP that require metabolic alteration for penetration. — *J. Raloff*

Birth-control vaccine safe in early tests

Clinical trials of an experimental birth-control vaccine reveal no major side effects, say researchers at the Flinders Medical Center in Adelaide, Australia. Injections of the vaccine, which triggers production of antibodies to neutralize a hormone necessary for pregnancy, left a few women with localized muscle pain but caused no general side effects.

Tests of the vaccine's ability to prevent pregnancy will come later. Ideally, one dose would last six months to a year, during which time antibodies would bind to human chorionic gonadotropin (hCG), making it impossible for a fertilized egg to implant in the uterine lining. To induce this immune response against a woman's own hormone, scientists developing the vaccine anchored a synthetically produced portion of the hCG molecule to diphtheria toxin, a combination capable of inducing strong antibody reaction against both substances. Since the antibodies target a hormone released by a fertilized egg, vaccinated women should have normal levels of other hormones and uninterrupted menstrual cycles, say the researchers in the June 11 LANCET.

Several weeks after the group injected varying doses of the vaccine into 30 surgically sterilized women, they found hCG antibodies in all 30. The question remains: How strong does the antibody reaction have to be to block pregnancy? Although primate tests have given a general idea, no one can be sure until the second phase of human trials, says the vaccine's developer, Vernon Stevens of Ohio State University in Columbus, who participated in the Australian study.

"The baboon studies are not exactly identical [to human studies]," Stevens says, adding that they have shown the vaccine to prevent pregnancy in animals.

Experimenting with a birth-control vaccine that uses the tetanus rather than diphtheria toxin to stimulate antibodies is G.P. Talwar of the All India Institute of Medical Sciences in New Delhi (SN: 6/7/86, p.365). Along with scientists at the New York-based Population Council, Talwar tested his version of the vaccine on 15 women in 1980, finding a weaker-than-expected antibody response to hCG.

One problem with previously tested hCG vaccines, Stevens says, was that women also formed antibodies against luteinizing hormone (LH), similar in shape to hCG. Inactive LH means disrupted menstrual cycles, and even early menopause in some cases. Since Stevens' vaccine uses a protein segment unique to hCG, women in the Australian study did not produce LH antibodies.

Stevens hopes to have U.S. efficacy tests underway next year. — *L. Beil*