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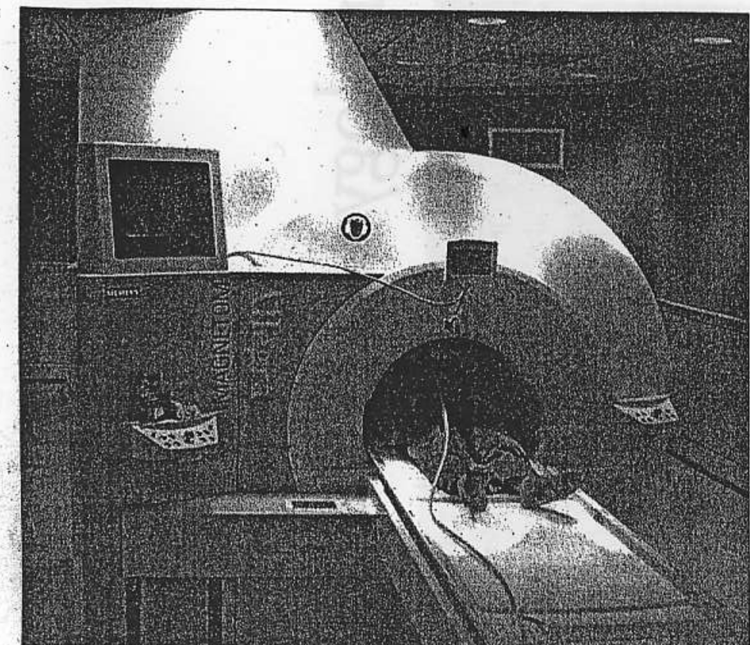
HEADS UP FOR BRAIN RESEARCH



The Siemens Allegra 3-tesla fMRI scanner will be used by University of Oregon researchers to study the brain. The machine is twice as powerful as standard MRI systems.

UNIVERSITY OF OREGON

Thanks to an array of grants from both government and private sources, the University of Oregon will soon have a souped-up MRI system dedicated to helping scientists further their knowledge of how the human brain operates

By **RICHARD L. HILL**
THE OREGONIAN

Getting into someone's head isn't easy. Scientists for centuries have been seeking to comprehend the workings of the human brain, our most complex organ.

The high-tech revolution, however, has produced new tools that allow brain scientists to examine the living, working brain in action. A powerful technology called fMRI — for functional magnetic resonance imaging — has become the rage in helping unravel many of the brain's mysteries.

That's why researchers at the University of Oregon are enthusiastic about the imminent arrival of their own fMRI machine.

The brain-imaging instrument, which combines ultra-high magnetic fields and radio waves, is scheduled to be installed on the Eugene campus next month as an integral part of the UO's Brain Biology and Machine Initiative. The research effort is bringing together an array of psychologists, biologists, physicists, computer and materials scientists and other researchers in investigating the brain as it processes thoughts and behavior.

With the scanner, scientists can conduct basic research and develop a better understanding of such tasks as language, perception and learning. The machine, dedicated purely for research, is one of only a few in the world being used outside a medical setting.

"This is a big step for us," said Helen J. Neville, a UO psychology professor who has had to go to other institutions to conduct brain studies using fMRI scanners. "This is a powerful machine that is dedicated exclusively to examining the functioning brain. We can use it to study the development of the brain and how it changes, along with such things as short- and long-term memory."

The new Siemens Allegra 3-tesla fMRI scanner will be placed in a new addition to Straub Hall, which houses the UO's highly regarded psychology department. An fMRI scanner is the psychologist's equivalent of a microscope turned inward, allowing a brain researcher to correlate physical processes with mental activities in precise detail.

Functional MRI works by measuring changes in blood flow during brain activity. When brain cells become active, blood flows to them, and the scanner registers increased oxygen in the activated area. The noninvasive tool gives scientists the ability to monitor changes in activity throughout the brain at about one-second intervals.

HOW AN fMRI SCANNER WORKS

Functional magnetic resonance imaging (fMRI) gives researchers a view of the working brain. It uses the combination of a powerful magnet and radio waves to see which parts of the brain are active. More blood flows to active parts of the brain. The blood carries oxygen, which alters the magnetic field in that area, and the change can be detected by the machine.

- In an fMRI system, a magnet surrounds the subject's head.
- Under appropriate conditions inside the magnet, the hydrogen atoms in the brain emit radio signals.
- The technique quickly generates large amounts of data. With fMRI, researchers can map the sites of brain activity to a resolution as fine as 1 millimeter, comparable to mapping a football field in 6-inch units.

IMAGE COURTESY DR. BRADLEY L. SCHLAGGAR/WASHINGTON UNIVERSITY, ST. LOUIS

An image shows the average brain activity of 40 children 7 to 10 years old who were speaking out loud, matching a verb to a noun.

RICHARD L. HILL, MICHAEL GUILLÉN/THE OREGONIAN

Magnetic field strength is measured in units called "teslas." A standard MRI system used primarily for medical procedures operates at 1.5 teslas, about 30,000 times stronger than the Earth's magnetic field. The new UO machine will be a 3-tesla system — twice as powerful — to give researchers more detailed images.

"With an fMRI, we acquire huge amounts of data every few seconds, because that's the kind of time frame we need to be looking at areas of the brain getting activated," said Ray L. Nunnally, a physicist who will direct the new brain-imaging facility. "The speed issue becomes very important, and that's why you need a strong magnet."

Nunnally hopes the scanner will begin to be used for research by the beginning of May after installation and tests are complete. Having a machine in their back yard will allow UO neuroscientists easy access to a powerful fMRI for long-term and shorter studies to get a picture of the mind in action.

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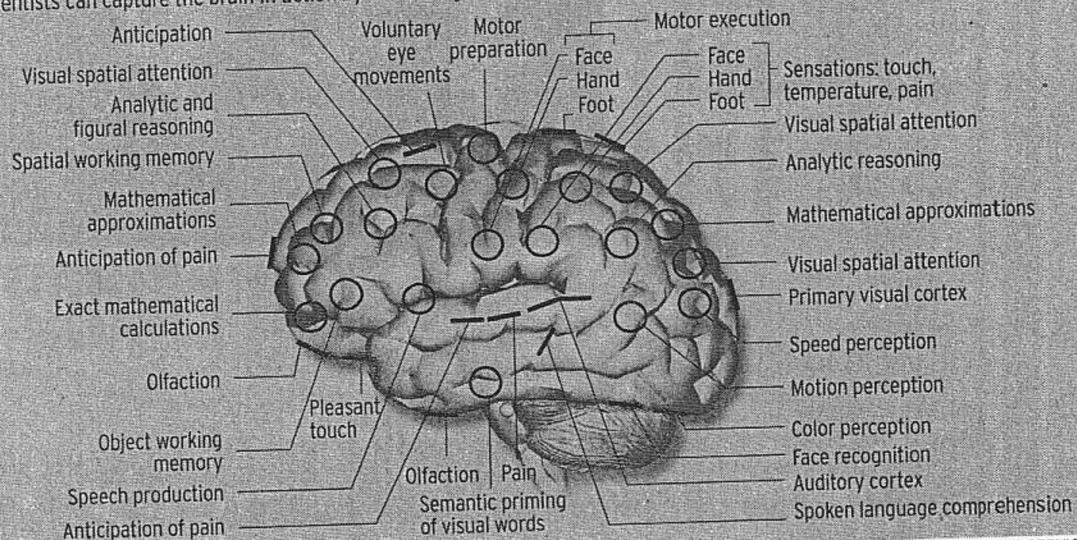
Brain: Technology has already brought results

Continued from Page B1

MAPPING THROUGH FUNCTIONAL MAGNETIC RESONANCE IMAGING (fMRI)

Scientists can capture the brain in action by measuring changes in cerebral blood flow.



NEW YORK TIMES NEWS SERVICE

Richard Linton, UO vice provost for research, said the machine will be a giant step in the Brain Biology and Machine Initiative. In the past few weeks, the program has received $1.8 million from Congress in its 2002 defense appropriations bill. Last year, UO alumni Robert and Beverly Lewis of Newport Beach, Calif., pledged $10 million for the university's neuroscience effort.

"We've had close to $15 million either committed or in hand for this program," Linton said. "Under the latest federal earmark, we would be working with the Army's Telemedicine and Advanced Technology Research Center." Previous financing has included $2.7 million from the Defense Department, $900,000 from the National Science Foundation and $500,000 in private money from the University of Oregon Foundation.

UO scientists are also hoping to acquire a powerful 9.4-tesla fMRI machine that would allow researchers to study the brains of small animals, such as lab mice and possibly even zebra fish, that are used in genetic and development studies. Linton said the machine would be more expensive — the one scheduled to be installed in February is about $2 million — because it would require a stronger magnet to obtain high-resolution images of the small brains. Part of the new federal money might go toward obtaining the second machine, he said.

Scientists have been using fMRI technology to study the brain for about the past decade. Findings in the past few months include:

◆ Vanderbilt University psychologists found that people who have been blind from birth use different parts of their brain when they read Braille than do those who lost their sight later in life. That difference sheds new light on the relationship between thought and language.

◆ Researchers at the University of Pennsylvania School of Medicine have found that telling a lie and telling the truth require different brain activities. Dr. Daniel Langleben, an assistant professor of psychiatry, said the small study might pave the way for improvements in lie-detection techniques.

◆ Dr. Bradley L. Schlaggar of the Washington University School of Medicine in St. Louis found that the brain-imaging technique works as well in children as in adults.

◆ Dr. Steven R. Pliszka, an associate professor of psychiatry at the University of Texas Health Center at San Antonio, found in preliminary tests that children with attention deficit hyperactivity disorder display a lack of activity in the right frontal lobe.

◆ Dr. Dean Shibata, assistant professor of radiology at the University of Washington, found that deaf people sense vibration in the part of the brain that other people use for hearing. The findings suggest that the experience deaf people have when "feeling" music is similar to the experience other people have when hearing music.

Don M. Tucker, a UO professor of psychology, plans to use the new machine to study emotions and their influences on memory and attention, along with such mental problems as anxiety disorders and depression.

Tucker wants to use the fMRI scanner with a brain-wave imaging device he developed that is an advanced version of the electroencephalogram, or EEG. The instrument, which consists of dozens of electrodes held against the scalp in an elastic net, delivers instantaneous views of the patterns of electrical activity within the brain.

The two techniques offer different pictures of the brain, Tucker said. The sensor array can detect extremely fast electrical signals that can't be picked up by the fMRI scanner. The fMRI machine, however, can better pinpoint the location of brain activity.

"We think if we can make some progress in comparing the two kinds of data, it would lead to some significant steps forward in understanding certain diseases, such as epilepsy," said Tucker, who is chief executive officer and chief scientist of Electrical Geodesics.

Tucker said one problem with using his system with an fMRI is that it's difficult to record electrical signals inside the magnet. He said a project is planned with the new fMRI scanner to determine how to combine the two techniques.

"This new facility is going to be a major breakthrough for the university," Tucker said. "It's a high-end system that is dedicated to research use, which is going to allow researchers from several fields to move ahead in their work."

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oceanographers, have supported the GRIP and GISP2 findings. By examining the presence of plankton that thrive at various temperatures, Lehman, Gerard Bond of Columbia University's Lamont-Doherty Earth Observatory and other researchers have been able to chart changes in temperature in the North Atlantic. The various groups have reported that the temperature record of the ice is echoed by the seafloor, suggesting that there are links between the temperature changes in the ocean and in the atmosphere.

The factors that cause the abrupt changes remain obscure. One theory holds that the heat-carrying capacity of the Atlantic Ocean—described as a conveyer belt—is somehow altered as fresh water is released by melting ice. These changes cause and are caused by changes in climate. Another hypothesis suggests that the conveyer is disrupted by global variations in rainfall.

For now, climate modeling is likely to offer only limited help in clarifying the reasons for the dynamic change. Although most models have found that doubling of carbon dioxide will result in a global temperature increase of 1.5 to 4.5 degrees Celsius, they are far from being able to incorporate all aspects of the climate system. "We are barely able to model the oceans; we cannot yet couple them with atmospheric models," Lehman says. Without a good model of these interactions, "the possibility of sudden changes is explicitly not allowed." Lehman goes on to note that one or two models have tried to include both elements: "And what do we get in them? Surprises."

So the Greenland findings, in sphinxlike manner, continue to pose questions. Were the changes local or global? If rapid fluctuations are the norm, why is the contemporary climate so stable? Could the accumulation of greenhouse gases trigger a dramatic, and potentially devastating, oscillation today?

"It is the biggest event this year," says Andrew J. Weaver of the University of Victoria in British Columbia, of the Greenland results. "The fact that interglacials are not times of stable climate," Bond adds, "is a warning that we are poised between modes and could bring on a switch." —*Marguerite Holloway*

Fractured Functions

Does the brain have a supreme integrator?

The brain, as depicted by modern neuroscience, resembles a hospital in which specialization has been carried to absurd lengths. In the language wing of the brain, some neurons are trained to handle only proper nouns, others only verbs with irregular endings. In the visual-cortex pavilion, one set of neurons is dedicated to orange-red colors, another to objects with high-contrast diagonal edges and still another to objects moving rapidly from left to right.

The question is how the fragmentary work of these highly specialized parts is put together again to create the apparent unity of perception and thought that constitutes the mind. This puzzle, known as the binding problem, has loomed ever larger as experiments have revealed increasingly finer subdivisions of the brain.

Some theorists have suggested that the different components of perceptions funnel into "convergent zones," where they become integrated. Among the most obvious candidates for convergent zones are regions of the brain that handle short-term, or "working," memories so that they can be quickly accessed for a variety of tasks. Yet two different sets of experiments done this year—one in which monkeys were monitored by electrodes and the other in which humans were scanned with positron emission tomography (PET)—show that the parts of the brain that cope with working memory are also highly specialized.

The monkey experiments were performed by Fraser A. W. Wilson, Séamas P. Ó Scalaidhe and Patricia S. Goldman-Rakic of the Yale University School of Medicine. The workers trained the monkeys to accomplish two tasks requiring working memory. In one task, each monkey stared at a fixed point in the middle of a screen while a square flashed into view at another location on the screen. Several seconds after the square disappeared, the monkey would direct its gaze to the spot where the square had been.

The other task required storing information about the content of an image rather than its location. The investigators flashed an image in the center of the screen. Each monkey was trained to wait until the object had disappeared and then turn its eyes left or right, depending on what type of object it had observed. Electrodes monitored the firing of neurons in the monkey's prefrontal cortex, a sheet of tissue that cloaks the top of the brain and has been implicated in mental activities requiring working memory.

In each test, a set of neurons started firing as soon as the image flashed on the screen and remained active until the task had been completed. But the "where" test activated neurons in one region of the prefrontal cortex, whereas the "what" test activated neurons in an adjacent but distinct region. "The prefrontal cortex has always been thought of as a region where information converges and is synthesized for purposes of planning, thinking, comprehension and intention," Goldman-Rakic says.

WASHINGTON UNIVERSITY

PET SCANS done at Washington University show certain regions of the brain engaged as a subject reads a list of nouns and suggests related verbs (left). *Different regions become active after the task is performed repeatedly with the same list* (center). *The original areas of the brain are reengaged when the subject is given a list of new nouns* (right).

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"We've shown that this area is just as compartmentalized as the sensory and motor regions."

Complementary findings described this year by investigators at Washington University have emerged from PET scans of humans. (PET measures neural activity indirectly by tracking changes in blood flow in subjects injected with a short-lived radioactive tracer.) In the experiments, volunteers were provided with a list of nouns. They were required to read the nouns aloud, one by one, and to propose for each noun a related verb. On reading the noun "dog," for example, the volunteer might suggest the related verb "bark."

When the subjects first did this task, several distinct parts of the brain, including parts of the prefrontal and cingulate cortex, displayed increased neural activity. But if the volunteers repeated the task with the same list of nouns several times, the activity shifted to different regions. When the volunteers were given a fresh list of nouns, the neural activity increased and shifted back to the first areas again.

The experiment suggests that one part of the brain handles the short-term memory requiring verbal invention and that another part takes over once the task has become automatic. In other words, memory might be subdivided not only according to its content but also according to its function. "Our results are consistent with Goldman-Rakic's ideas," comments Steven E. Petersen, a member of the Washington University team.

So how do all the specialists of the brain manage to work together so smoothly? Are their activities coordinated by a central office or through some form of distributed network? Petersen favors "a localized region or a small number of localized regions," where perceptions, memories and intentions are integrated. Goldman-Rakic is leaning toward a nonhierarchical model in which "separate but equal partners are interconnected, communicating with each other."

Larry R. Squire, a memory researcher at the University of California at San Diego, thinks the binding problem may take many years to solve. He concedes that "we still don't really have a clue" as to what the binding mechanism is. But he is hopeful that the answer will inevitably emerge, given the rapid advances in techniques for studying the brain—including microelectrodes, noninvasive imaging technologies (such as PET and magnetic resonance imaging) and computers, which can help make coherent models out of empirical data. "We need it all," Squire says. —*John Horgan*

 8 Aug 97

Brain needs a break for new skills to take

Research finds new physical skills need time to be encoded permanently, and going on to something else may erase them

By PAUL RECER
The Associated Press

WASHINGTON — After learning a new physical skill, such as riding a bike, it takes six hours to permanently store the memory in the brain.

But interrupt the storage process by learning another new skill and that first lesson may be erased, according to research into memory and the mind.

"We've shown that time itself is a very powerful component of learning," said Dr. Henry H. Holcomb, a psychiatrist who heads a Johns Hopkins University group that studies how people remember.

"It is not enough to simply practice something. You have to allow time to pass for the brain to encode the new skill."

The researchers used a device that measures blood flow in the brain. They concluded it takes five to six hours for the memory of a new skill to move from a temporary storage site in the front of the brain to a permanent storage site at the back.

During those six hours there is a neural "window of vulnerability" when the new skill easily can be eroded from memory if the person attempts to learn a second new skill, Holcomb said.

"If you were performing a piano piece for the first time and then immediately started practicing something else, then that will cause problems in retention of the initial piece that you practiced," he said.

It would be better if the first practice session were followed by five to six hours of routine activity that required no new learning.

A report on the study is to be published today in the journal Science.

"This is a new and important insight into the relationship between motor skill learning and neural activity," said Dr. Carolyn B. Cave, a psychologist and learning researcher at Vanderbilt University.

She cautioned, however, that not enough is known to identify precisely how the successive learning of different skills could interfere with one other.

In the Hopkins study, the researchers used a positron emission tomography device, or Pet, to measure blood flow in the brain of test subjects while they learned a motor skill.

The people were placed in the devise and then taught to manipulate an object on a computer screen by using a motorized robot arm. The test required unusually precise and rapid hand movements that could be learned only through practice.

During this learning process, the device's image showed that blood flow was most active in the prefrontal cerebral cortex of the brain.

After the learning session, the test subjects were allowed to do unrelated routine things for five to six hours, then were retested.

When operating the robot arm this time, the blood flow was most active in the posterior parietal and cerebella areas, Holcomb said.

"This shift in the brain is necessary to render the memory invulnerable and permanent," he said. "What we see is the consolidation of the memory."

It is such a consolidation that allows a person to never forget some skills, such as riding a bike or swimming, learned as a child.

Some of the Hopkins test subjects were trained in a new motor task immediately after learning the first skill. Later, those subjects were tested on how much of the first lesson they remembered — and had lost much of the skill they had learned first.

"If we teach one task and then immediately introduce a new task, we know that will largely erase any learning gained from the first task," Holcomb said.

"But if we wait five to six hours and then give them a new task, then we don't erase what was learned in the first lesson."

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Research Notes: Language Learning and the Developing Brain

"Gray Matters: The Developing Brain" is a public radio program that was recently broadcast by Public Radio International and produced in association with the Dana Alliance for Brain Initiatives, an independent, non-profit organization made up of over 140 of the nation's leading brain scientists. The content of the program, which focused on how the young brain develops into a "reading, writing, and rollerblading 10-year-old," and which addressed early language learning, is reported here.

The child's brain is different from the adult brain in that it is a very dynamic structure that is evolving. A two-year-old child has twice as many synapses (connections) in the brain as an adult. The young brain must use these connections or lose them. Thus, failure to learn a skill during a critical or sensitive period has important significance. According to Dr. Michael Phelps, Chairman of the Department of Molecular and Medical Pharmacology of the UCLA School of Medicine, the learning experiences of the child determine which connections are developed and which will no longer function.

Dr. Patricia Kuhl, a Speech Scientist at the University of Washington, reports that babies are born "citizens of the world" in that they can distinguish differences among sounds (temporal, spectral, and duration cues) borrowed from all languages. They are ready to learn any language they hear, but by six months of age, they start to specialize in their native language.

Dr. Susan Curtiss, Professor of Linguistics at UCLA, who studies the way children learn languages, notes that in language development there is a window of opportunity in which the child learns the first language normally. After this period, the brain becomes slowly less plastic and by the time the child reaches adolescence, the brain cannot develop "richly and normally any real cognitive system, including language."

The four- or five-year old learning a second language is a "perfect model for the idea of the critical period." According to Dr. Curtiss:

> ...the power to learn language is so great in the young child that it doesn't seem to matter how many languages you seem to throw their way....They can learn as many spoken languages as you can allow them to hear systematically and regularly at the same time. Children just have this capacity. Their brain is just ripe to do this....there doesn't seem to be any detriment to... develop(ing) several languages at the same time.

When children wait until high school to start studying a foreign language, the job is much harder. The task now involves learning the rules of grammar, translating, reading, and trying to develop language learning strategies. The task is a different one than it was for the young child in the sensitive period for language learning. Brain plasticity has been lost, the number of synapses has greatly reduced, and the brain no longer has the same facility to restructure itself that it had when the child was young.

"Gray Matters: The Developing Brain" is available from: Wisconsin Public Radio Assoc., The Radio Store, 821 University Ave., Madison, WI 53706-1497; 1-800-652-7246. Audiocassette (for 40-minute program) \$8.00; transcript \$6.00; shipping \$3.00.

"Even in late childhood...one cannot learn a first language fully or naturally or normally." (Dr. Susan Curtiss)

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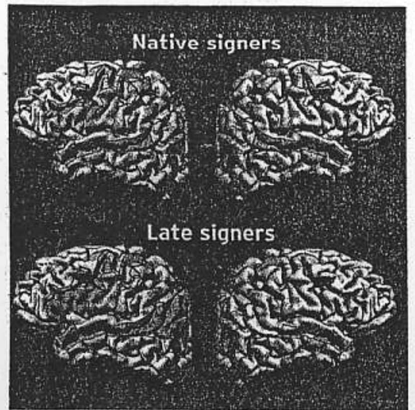

UNIVERSITY OF OREGON/NATURE NEUROSCIENCE

Images made with an fMRI machine show differences in brain activity between early learners of American Sign Language and later learners as they respond to signing gestures. Like English, American Sign Language activates extensive regions of the left hemisphere (left), but activates a different, larger region of the right hemisphere in native signers than in later-learning signers (right).

Early sign learners call on different brain cells

Scientists note that the areas of the brain that are active when one is signing depend on the age sign language was learned

By RICHARD L. HILL
THE OREGONIAN

Scientists studying the brain activity of people who use American Sign Language have found the first evidence that there is a crucial period for acquiring a nonverbal language, just as there is for spoken languages.

Scientists from the University of Oregon, the University of Washington and two other institutions found that the patterns of brain activity differed in people who learned sign language early in life compared with those who learned it after puberty. The findings were reported this month in the journal Nature Neuroscience.

Aaron J. Newman, the study's lead author and a UO psychology student working on his doctorate, said the research team used functional magnetic resonance imaging, or fMRI, to examine brain activity in 27 participants. All of the subjects could hear and speak English. Of those, 16 were born to deaf parents and learned both English and sign language early in their lives. The other subjects did not learn sign language until early adulthood.

> *"...the motivation of the study was to see whether there were any obvious differences in the brain activity between the early learners and later learners."*
>
> AARON J. NEWMAN, STUDY'S LEAD AUTHOR AND UO PSYCHOLOGY STUDENT

While images of their brains were being taken, the participants watched a screen and were asked to read written English sentences and American Sign Language sentences.

"We know from other studies that people who learn sign language later in life tend not to do as well with it," said Newman, the study's lead author. "So the motivation of the study was to see whether there were any obvious differences in the brain activity between the early learners and later learners."

OMSI will get into the heads of visitors with brain exhibit

A new traveling exhibit about the brain will open Jan. 26 at the Oregon Museum of Science and Industry.

"Brain: The World Inside Your Head" is a hands-on look at the human body's most complex organ. The 5,000-square-foot exhibit uses virtual reality, video games, optical illusions and interactive displays to explore the brain.

Designed for adults and children, the exhibit explains the brain's geography and how the organ functions. Visitors can enter the electrical workings of a simulated human brain; "open" the brain to understand the functions of its areas; see how the brain changes throughout a lifetime; and visit a 19th-century laboratory to find out how early researchers developed knowledge about the brain.

In the exhibit's closing section, visitors will find materials on brain-based diseases and disorders that they can take home with them to learn more about the issues facing their families and friends. Brain-based diseases and disorders — such as depression, schizophrenia, Alzheimer's and Parkinson's — also are discussed.

The national tour of "Brain: The World Inside Your Head" is made possible by Pfizer. The exhibit was produced by BBH Inc. with the National Institutes of Health. AT&T is the exhibit's local presenting sponsor.

The exhibit will run through May 5.

Sign: Research aims at neural foundation

Continued from Page B1

Newman said they found an area in the brain's right hemisphere — the right angular gyrus — that was consistently activated by sign language in participants who had learned it from shortly after birth. The area was not consistently activated among late signers.

The study indicates there is a need for childhood exposure to languages, including American Sign Language, because the brain apparently does not adapt to language in the same way in adulthood, the researchers said.

"This work is important because we want to understand the neural systems underlying language," said professor and one of the study's researchers. "We want to know whether they are malleable or fixed and the degree to which they may vary in different languages."

The brain images were obtained using an fMRI machine at the National Institutes of Health in Bethesda, Md., Newman said. Other members of the research team were Helen J. Neville, a UO psychology professor; Daphne Bavelier, a professor of brain and cognitive sciences at the University of Rochester; and Peter Jezzard, a physicist at John Radcliffe Hospital in England.

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