yield nuclear weapons has not been "categorically" ruled out as a counterproliferation tool. Dubbed "mininukes," such weapons would have yields ranging from five kilotons to 100 tons. (The bomb that destroyed Hiroshima had a yield of 10 kilotons.) Indeed, some officials in the weapons laboratories, notably Edward Teller of Lawrence Livermore National Laboratory, have suggested that mininukes deployed on high-precision missiles would make effective counterproliferation weapons. In addition to serving as "bunker-busters" or electromagnetic-pulse bombs, mininukes would be ideal for destroying biological-weapons stockpiles, researchers say, because the thermonuclear heat and radiation would kill and not just disperse pathogens.

In last year's Defense Authorization Bill, Congress specifically prohibited the Department of Energy from conducting "research and development which could

Neural Eavesdropping

How does the brain establish and store memories? Neuroscientists have traditionally addressed this question by focusing on neurons and the synapses that link them—just as engineers might try to understand how homes in a town communicate simply by tracing the telephone lines linking them. Now investigators must consider the possibility that each home's windows are wide open and that everyone is eavesdropping on his or her neighbors.

The new findings involve a neural mechanism called long-term potentiation (LTP), which is thought to play a crucial role in memory and learning. The effect occurs when repeated transmissions of impulses across the synapse linking two neurons result in a positive feedback effect, making future transmissions still easier. Donald O. Hebb, the great Canadian psychologist, first proposed the existence of an LTP-type mechanism 40 years ago.

Many researchers assumed that for LTP to occur, a signal must be sent from the postsynaptic neuron (which receives the impulse) back to the presynaptic neuron (which originally sent the impulse) to strengthen the bond between them. The hypothetical signal has been named the retrograde messenger.

Several years ago a number of workers, notably Daniel V. Madison and Erin M. Schuman of Stanford University, performed experiments suggesting that the retrograde messenger might be nitric oxide. Nitric oxide is a soluble gas so reactive that it generally does not last for more than a few seconds. Moreover, it slips easily in and out of cellular membranes, traveling without regard for normal channels of communication.

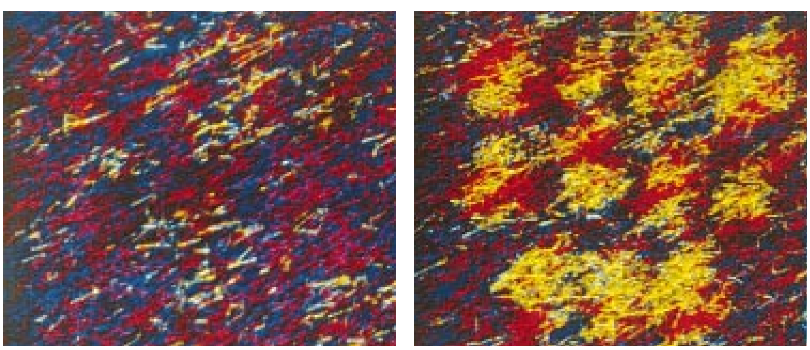
Yet Madison and Schuman wondered: If nitric oxide diffused from the postsynaptic cell to the presynaptic one, might it affect neighboring synapses as well? If true, that hypothesis would disprove the presumption—key to Hebbian learning—that LTP occurring at one synapse has no effect on neighboring ones. The view that LTP would be synapse specific "was the dogma," Schuman says.

Actually, evidence that LTP might not be entirely localized had been presented in 1989 by workers at the Max Planck Institute for Biological Cybernetics in Tübingen. When they evoked potentiation in one synapse of a neuron taken from the hippocampus of a rat, potentiation was reinforced in nearby synapses. At that time, many investigators felt the results were not robust enough to overturn the accepted view.

Madison and Schuman repeated the Germans' experiments using better instrumentation and tighter controls and got the same results. They then showed that nitric oxide contributed to the effect. When they applied a chemical that blocked the production of nitric oxide in a postsynaptic neuron, long-term potentiation failed to occur either in that synapse or in neighboring ones.

Madison and Schuman emphasize in *Science* that nitric oxide may be just a link in a chain generating the diffusion effect. Yet signs of nitric oxide's extracellular activity continue to accumulate. Three weeks after Madison and Schuman's paper appeared, a group led by P. Read Montague and Michael J. Friedlander of the University of Alabama announced in *Science* that nitric oxide can mediate interactions between neural pathways that are not directly connected.

To Eric R. Kandel of Columbia University, an authority on the molecular basis of memory, the message of all this work is clear: the old Hebbian model of learning, which ignores the extracellular context of communication, is too simple. "This is the most oversold idea in neuroscience," Kandel proclaims. Indeed, the new findings lend weight to a non-Hebbian theory proposed in 1990 by Montague and two colleagues, Joseph A. Gally and Gerald M. Edelman of the Neurosciences Institute in New York City. In the model, called volume learning, the diffusion of nitric oxide contributes not only to memory formation but also to the spatial organization of the brain during embryonic development. The putative effects would stem from nitric oxide's well-known ability to dilate blood vessels as well as its role as an enhancer of neural connections.



Cerebral Cortex May/June 1991

VOLUME-LEARNING simulation shows how the diffusion of nitric oxide might result in enhanced neural connections in localized regions of the brain.

Terrence J. Sejnowski of the Salk Institute for Biological Studies in San Diego thinks volume learning may explain why neurons gather into onionlike sheets and columnar structures in certain regions of the brain. The width of the layers and the columns are roughly equal to the effective range of a diffusing nitric oxide signal. Yet Sejnowski expects that upcoming experiments will reveal that nitric oxide is only one actor in a complex drama. "It seems," he observes, "that there is a whole family of diffusion messengers, each with its own targets and time course, that contribute to plasticity and development." —*John Horgan*