Staggering mice and the maturation of nerve cell glue

Rockefeller University scientists have linked defective maturation of a substance called nerve cell adhesion molecule (N-CAM) with a genetic abnormality that causes mice to stagger. The finding suggests a role for this cell surface molecule in the development of the brain.

In work over the last decade on nerve cells growing in laboratory dishes, Gerald Edelman and colleagues have found that N-CAM mediates the association of nerve cells in vertebrates, including man. "These molecules are not present in other tissue and recognize only themselves," Edelman told SCIENCE NEWS.

"N-CAM is a large protein found on the surface of nerve fibers which interacts with itself and allows the fibers to form straight and branching structures. When N-CAM is blocked by an antibody, the patterned and branched system of nervous tissue falls into a tangle resembling a bowl of spaghetti," report Edelman and colleague Bruce Cunningham.

The adhesion molecule is unusual because it contains large amounts and an unusual pattern of a negatively charged sugar called sialic acid. The scientists find that N-CAM of an embryonic mouse differs from that of a normal adult. The embryonic mouse N-CAM contains three times as much sialic acid. This difference is likely to alter the cells' binding properties, Edelman says.

Edelman and Cheng-Ming Chuong have examined N-CAM in the brains of mutant mice with behavioral disorders. The mice called staggerer have abnormal motor coordination and gait and they also have defective nerve cell development in the brain area called the cerebellum. Edelman and Chuong report in the November PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES that in staggerer mice the N-CAM in the cerebellum remains in its embryonic form, as identified with monoclonal antibodies and with gel electrophoresis. Edelman and Chuong suggest the embryonic N-CAM allows nerve cells and their processes to migrate beyond normal limits and thus miss their normal interactions. Edelman says these findings are the first demonstration of a possible role of N-CAM in whole living animals.

Edelman, who won a Nobel prize for work on antibodies in 1972, suggests that N-CAM plays a role in the intricate pattern of nerve cell connections that develop in the brain. He envisions numerous variations in the number and arrangement of attached sugars directing how cells associate. These variations would not be genetically determined but would develop according to enzyme activity levels in the environment surrounding a cell.

"The beauty of the idea is that it repeats the concept Edelman contributed to immunology," says Richard Sidman of Harvard Medical School, who with associates at the Jackson Laboratory in Bar Harbor, Maine, first discovered staggerer mice 20 years ago. "The idea is that the extraordinarily complex group of connections in the nervous system, like the extraordinary range of immune response, is controlled by a single class of molecule."

While other scientists accept that N-CAM plays a role, if not the "key" role Edelman claims, in nerve cell adhesion, many are skeptical of the proposed role in directing specific patterns, even calling it bizarre and outrageous.

"[N-CAM] is a really fascinating protein. It's got to have some important function," says Paul Patterson of Harvard Medical School. "We don't know if it's just a glue or something more interesting with real information content. It would be most exciting if it were heterogeneous, having different forms in different places on different neurons. But there isn't evidence. No one really is sure what its role is."

—J.A. Miller

White House backs federal aero R&D funds

In what amounts to a substantial turnaround from its position of a year ago, the Reagan administration has now urged that the federal government continue to support aeronautical research and development for civilian needs, not just for defense. A report from the White House's Office of Science and Technology Policy recommends that the National Aeronautics and Space Administration keep up its present role of funding and conducting civil aeronautics research, as well as aiding military programs.

Congressman Dan Glickman (D-Kan.), chairman of the House subcommittee whose domain includes aviation, speaks favorably of the report's conclusions, but maintains that "it is necessary to set the record straight on the administration's trumpeting of its new aeronautical policy. We should not forget that the Office of Management and Budget began the year with an ill-conceived idea of gutting the NASA aeronautics program. The reason, aside from their simple budget-cutting zeal, lies in the ivory-tower notion that industry could and should do it alone."

Indeed, in announcing the new policy, OSTP director (and presidential science adviser) George A. Keyworth II had already acknowledged the change in attitude from when the administration's fiscal 1983 budget plan was being prepared late last year. "Quite honestly," he said in a recent speech to the Aero Club of Washington, "there was a widespread notion that, after decades of federal support, we might be at a point of diminishing returns. Perhaps it was time for the federal government to cut back on non-military aeronautics research that might more appropriately be done by industry. Let me assure you that we were very close to substantially changing the federal role in aeronautics."

The anticipation of severe repercussions in the huge U.S. aviation industry, he said, prompted the administration to put off any major reductions for another year while the federal role was more carefully evaluated. According to Keyworth, "It's a good thing we waited."

Glickman takes a rather different view. "Fortunately," he says of the earlier aeronautics cutback proposed by OMB, "Congress wasn't fooled, and much of OMB's cut was restored. Without this show of strength, I seriously doubt if Dr. Keyworth would have been allowed to come out with the strong conclusions in his study."

For strong they are, at least by contrast with the idea of eliminating any federal role in civilian aeronautics research. The report recommends that both industry *and* government continue to "maintain an environment in which civil aviation services and manufacturing can flourish." Additionally, they should "ensure the timely provision of a proven technology base to support future development of superior U.S. aircraft."

A major concern in the U.S. aircraft industry has been growing competition from foreign manufacturers, and preserving a competitive edge is an acknowledged factor in the OSTP report. "Our findings," says Keyworth, "clearly showed that aero R and T [research and technology] is still at the science frontiers; there's clear potential for excellent new research." The problem, he acknowledges, is that it is very difficult for industry to justify the risk of investing in research programs whose payoffs may be years away, "because they can't capture the benefits for themselves. As a consequence," he says, "we see no alternative but continued government support if we expect to maintain the level of research and technology demanded by national interests."

The report basically recommends maintaining the organizational status quo, with the Defense Department handling military development programs while NASA conducts research efforts that address both civil and military needs.

"More important, however, than pointing out that the administration reinvented the wheel," says Glickman, "is what comes next. The public and the Congress will be anxiously waiting to see whether the administration's new-found policy statement will be followed by firm action ... or whether it will take a 'namby-pamby' approach with all talk and no action."

—J. Eberhart