

## Apo E in Alzheimer's stunts nerve growth

Many researchers agree that a molecule called apolipoprotein E (apo E) is somehow linked to the development of Alzheimer's disease (SN: 1/1/94, p.8). But they have yet to figure out why inheriting one form of this molecule increases an individual's risk of developing the debilitating dementia. Many people with apo E-IV are more likely to show symptoms of Alzheimer's at younger ages than people who inherit other forms.

Now, experiments involving peripheral nerve cells of rabbits have revealed a key difference between apo E-IV and the more common isoform known as apo E-III in regulating the growth of young nerve cell appendages, or axons. Apo E-III stimulates this growth; apo E-IV does not, says Robert W. Mahley, a cellular and molecular biologist at the Gladstone Institute of Cardiovascular Disease at the University of California, San Francisco.

Mahley and his colleagues had begun studying apo E molecules long before genetic studies linked different forms of apo E to Alzheimer's disease. His group had learned that cholesterol-rich lipoprotein particles stimulate the growth of branches from developing axons. These researchers then observed that adding apo E-III to laboratory dishes of nerve cells causes axons to grow longer rather than to branch.

Substituting apo E-IV for apo E-III, however, stunts both types of axon growth, report Mahley, Gladstone's Britto P. Nathan, and their colleagues in the May 6 SCIENCE. "We find quite a striking difference [between the two]," says Mahley. In addition, unpublished work by this team suggests that apo E-IV leads to denser deposits of the beta-amyloid peptide implicated in Alzheimer's disease.

"To us, the [Gladstone] work is important because it demonstrates that there are isoform-specific effects on the development and growth of neurites [young axons]," comments Warren J. Strittmatter, a neuroscientist at Duke University Medical Center in Durham, N.C.

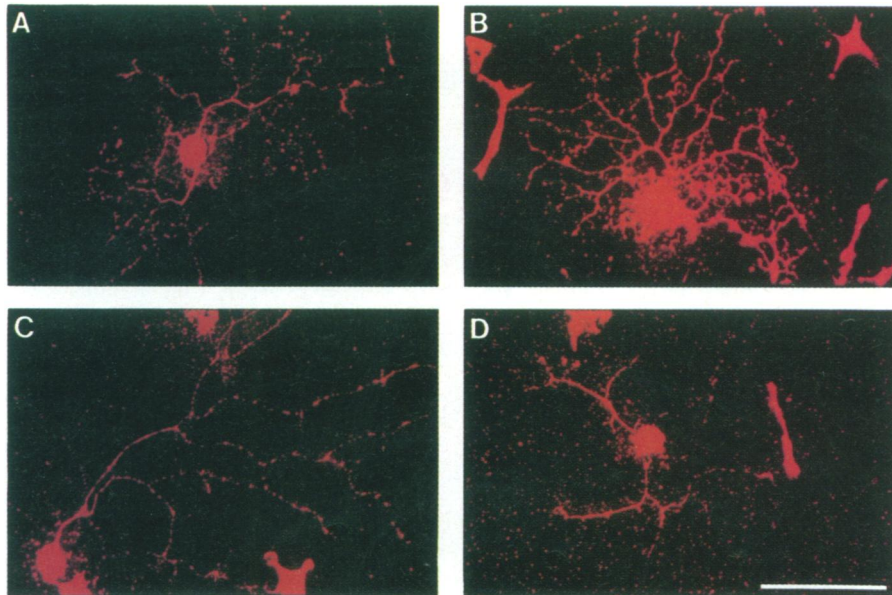
A Duke group has suggested that apo E-IV somehow fails to protect nerve cells in the same way that apo E-III can and therefore does not slow the progressive loss of brain function that eventually leads to Alzheimer's.

"This [report] could give insight into the neuronal mechanism," says Zaven S. Khachaturian of the National Institute on Aging in Bethesda, Md. The brains of people with apo E-IV may be less able to maintain or repair vital links between nerve cells.

When peripheral nerves are injured, white blood cells nearby make lots of apo E so they can take up lipids released by the deteriorating nerve cells, Mahley explains. Those lipids help rebuild nerve tissue. In addition, apo E-III may help

cells construct and maintain microtubules, which make up an intracellular freight system for shuttling molecules to the far reaches of axons. By not playing that role, apo E-IV may impair nerve cells, Mahley and Strittmatter suggest.

In these experiments, apo E's effects depend on the presence of lipid particles.



Nerve cells grown alone (a), with cholesterol-rich particles (b), and with particles plus apo E-III (c) or apo E-IV (d) show how apo E affects the growth of nerve endings.

Nathan et al./SCIENCE

## Temperatures on the rise in deep Atlantic

While retracing Columbus' route across the Atlantic, an international group of scientists detected a substantial warming in the subtropical part of that ocean. Water temperatures at some depths have increased by as much as 0.32°C since the late 1950s, a finding roughly in keeping with predictions about global greenhouse warming, according to the research team.

"That's a huge signature and certainly warrants further monitoring," says one of the project participants, Robert Millard of the Woods Hole (Mass.) Oceanographic Institution. Gregorio Parrilla of the Spanish Oceanographic Institute in Madrid served as chief scientist on the cruise. The investigators report their findings in the May 5 NATURE.

Sailing on a Spanish naval ship in the summer of 1992, the oceanographers followed the latitude line of 24°N, taking measurements every 60 kilometers. Other teams had traveled the same route in 1957 and in 1981.

During the 1981 expedition, researchers discovered that the western portion of the Atlantic had warmed by as much as several tenths of a degree Celsius since 1957. Between 1981 and 1992, however, the central and eastern parts of the

ocean warmed and the western third cooled slightly. Over the full 35-year period, temperatures increased across the entire 24°N band of the Atlantic. Most of the warming was concentrated between the depths of 700 and 2,500 meters.

The oceanic warming generally resembles the pattern expected to develop as a result of increased greenhouse gases in the atmosphere. But the two do not match exactly. Although computer models suggest that temperatures in the surface waters should increase the most, actual observations show a combination of warming and cooling there.

Ronald J. Stouffer of the National Oceanic and Atmospheric Administration's Geophysical Fluid Dynamics Laboratory in Princeton, N.J., says measurement differences may account for the lack of pronounced surface warming. The three expeditions traveled at different times of year, and the temperature at the top of the ocean varies dramatically from season to season.

Stouffer and others note that natural climatic variations could have caused some or all of the ocean warming. Then again, greenhouse gases could be the culprit. For now, scientists can't apportion the blame.

— R. Monastersky