Amyloid Can Trigger Brain Damage

Autopsies of Alzheimer's patients show waxy plaques of a protein called beta-amyloid littering the brain like shrapnel on a battlefield. Yet researchers have failed to establish whether beta-amyloid actually causes the disease.

Now, a study of monkeys shows that beta-amyloid can indeed damage nerve cells, or neurons, in the brain, especially in older animals.

Some researchers have suggested that an accumulation of amyloid plaques over many years contributes to Alzheimer's disease, which would help explain why the condition usually strikes the elderly. The new study, however, shows that equal amounts of beta-amyloid inserted into the brains of young and old monkeys are far more destructive in the old ones. The work appears in the July NATURE MEDICINE.

"This animal model shows that beta-amyloid introduced into the brain at levels similar to that in Alzheimer's disease can actually cause brain cell death," says coauthor Bruce A. Yankner, a neurologist at Harvard Medical School and Children's Hospital in Boston.

The study suggests a "two-hit" pattern in Alzheimer's disease in which plaque accumulation combines with "some other age-related process that is poorly defined as of yet," says Ted M. Dawson, a neurologist at Johns Hopkins Medical Institutions in Baltimore. "It's an interesting paper."

Alzheimer's disease is the most common form of neurological impairment in the elderly, affecting about 4 million people in the United States. Short-term memory and attention often falter first, followed by language, abstract reasoning, judgment, and insight.

"I think certain protective factors [against beta-amyloid plaque] that we have as young adults gradually vanish with middle age and old age," Yankner says. These traits don't always endure into old age in the population because they would not impart any selective evolutionary advantage, he speculates.

Some Down's syndrome patients develop plaques early in life but suffer no significant neuronal loss and cognitive decline from them until middle age. The finding that beta-amyloid unleashes its toxicity only in aged brains could explain this observation, Yankner says.

To assess how the effect of beta-amyloid varies with age, the researchers placed small amounts of the protein into the brains of rhesus monkeys, marmoset monkeys, and rats. After 11 days, they looked for three kinds of damage: destruction of neurons; harmful proliferation of microglia, small cells that act as part of the brain's support structure; and chemical changes in tau protein, which can contribute to the tangles typically found in Alzheimer's patients' brains (SN: 6/20/98, p. 389).

Postmortem examinations showed that four rhesus monkeys aged 25 to 28 years each incurred much more of all three forms of brain damage than either of two 5-year-olds. All five older marmosets tested, aged 8 to 10 years, also showed considerable neuronal damage, compared with five other marmosets only 2 or 3 years old.

Moreover, the old rhesus monkeys experienced considerably more brain damage than the old marmosets. By contrast, the old rats in this study, aged 24 to 26 months, were largely unaffected by beta-amyloid, Yankner says. Rats rarely live more than 3 years.

While the findings establish that beta-amyloid is toxic to aged but not young primates' brains, they also suggest that animals with long life spans may be at greater risk from the protein than those that lead short lives.

Scientists have puzzled over earlier research in which rodents didn't experience brain damage from beta-amyloid plaque. Such results had cast doubt on the idea that the plaques cause the dementia associated with Alzheimer's disease in humans. The new study establishes that the dangers of beta-amyloid are species-specific, very weak in rats but strong in primates, particularly higher ones. —*N. Seppa*

Monopole search comes up empty-handed

Positive and negative electric charges can exist separately. The same can't be said of the north and south poles of a magnet. Breaking a bar magnet in half, for example, produces two smaller magnets, both with north and south poles. Indeed, it appears impossible to obtain an isolated north or south magnetic pole.

The apparent absence of a single magnetic charge, or monopole, makes the physical laws governing electricity somewhat different from those that govern magnetism. This lack of symmetry has long bothered physicists, prompting much theoretical work and a number of extensive searches for evidence of monopoles (SN: 11/27/82, p. 348; 10/5/91, p. 219).

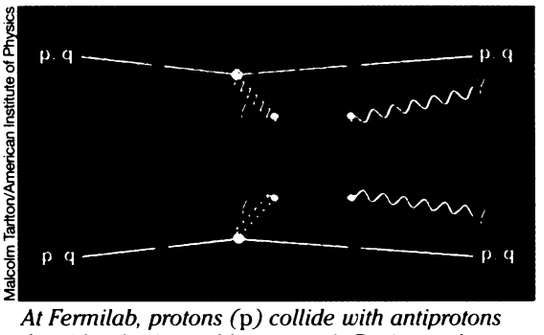
Now, a team of physicists using the D0 detector at the Fermi National Accelerator Laboratory (Fermilab) in Batavia, Ill., reports no sign of magnetic monopoles in the debris of high-energy collisions between protons and antiprotons at the Tevatron accelerator.

The new results exclude the existence of magnetic monopoles over a broad range of particle masses, the researchers conclude in a report to be published in PHYSICAL REVIEW LETTERS.

In 1931, Paul A.M. Dirac showed that the existence of magnetic monopoles would help explain why electric charge comes in multiples of the charge on an electron. He predicted that monopoles would strongly scatter photons.

Checking for energetic photons, Fermilab physicists found none that could be attributed to interactions with monopoles. Their measurements would have detected any magnetic monopoles having a mass (expressed in energy units) less than 600 billion electronvolts (GeV).

That's no surprise, says Gordon L. Kane of the University of Michigan in Ann Arbor. If they exist, monopoles are likely to be extremely heavy and rare. —*I. Peterson*



Malcolm Tarlton/American Institute of Physics

*At Fermilab, protons (*p*) collide with antiprotons (*p *with a horizontal bar on top). During such a collision, a single quark (*q*) within the proton may interact with a single antiquark (*q*-bar) within the antiproton. That interaction is sometimes accompanied by the emission of extremely short-lived particles known as virtual photons (*γ *on left). Theorists predict that an encounter between virtual photons and heavy magnetic monopoles (*M*) would produce a pair of energetic, potentially detectable photons (*γ *on right).*