rons as well. If so, this inflammatory activity, which could be triggered by any number of factors, could create a vicious spiral of nerve cell death until dementia ultimately set in.

McGeer reasoned that if he was right, individuals with autoimmune diseases such as rheumatoid arthritis, who take anti-inflammatory drugs over long periods of time, should have a reduced incidence of Alzheimer's disease. So with Rogers, whom he had met at a conference at Cold Spring Harbor in 1988, and who had independently been investigating immunological mechanisms in Alzheimer's disease, McGeer conducted a retrospective study of Alzheimer's incidence in rheumatoid arthritis patients and of rheumatoid arthritis incidence in Alzheimer's patients. Using Canadian and American hospital data covering more than 12,000 patients older than age 64, McGeer and Rogers found what appeared to be an abnormally low number of patients who had been diagnosed with both diseases. For example, only 0.39% of those diagnosed with rheumatoid arthritis had also been diagnosed with Alzheimer's, whereas in the general population, the same age group had an Alzheimer's prevalence of 2.7%. Not long afterward, the two researchers found their hypothesis bolstered by a similar study, reported in the British *Journal of Rheumatology* in 1989 by a group of physicians in London.

But there is at least one contradictory study. In 1991, researchers at the Mayo Clinic in Rochester, Minnesota, led by epidemiologist Mary Beard, found an apparently normal incidence of Alzheimer's in patients treated at the Mayo Clinic who had been diagnosed as having rheumatoid arthritis. The reason for the discrepancy is unclear.

PATRICK MCGEER

Double whammy? Senile plaques show β-amyloid *(brown color)* and agglomerations of reactive microglia *(purple)*, which contribute to inflammatory responses.

In any case, 1991 brought additional evidence in favor of the inflammatory hypothesis from an unexpected source. Nobuo Harada, a local government health official, noted what appeared to be an extremely low incidence of dementia in a leper colony on the island of Nagashima. Following up on that observation, McGeer, Harada, and several Japanese colleagues performed a study in about 4000 aged Japanese leprosy patients. The result: The incidence of dementia was only 2.9% in those taking the leprosy drug dapsone, which also has anti-inflammatory effects, but 6.25% among those who had not taken the drug for 5 years. Another group of Japanese researchers, led by Yoshio Namba at the Tokyo Institute of Psychiatry, analyzed the autopsied brains of 16 leprosy patients, all of whom had probably been treated with dapsone. They found an unusual absence of senile plaques in the leprosy patients' brains compared to those of age-matched controls.

Even if Rogers and McGeer's supposition that inflammation in the brain contributes to Alzheimer's development is correct, it would not rule out a role for β-amyloid. Aggregated β-amyloid may kill nerve cells directly as many researchers now think. But in addition, McGeer and Rogers suggest, the protein may also play an integral part in the inflammatory response in the brain. Last year, cooperating with Neil Cooper's group at the Scripps Clinic and Lieberburg's at Athena, they showed that aggregated β-amyloid activates the cell-killing complement proteins. "I would say β-amyloid is probably modestly toxic by itself in a compacted form, and probably very toxic when it has attracted the immune system," Rogers concludes.

Moreover, although most researchers think that nerve cells are the major source of the brain's β-amyloid deposits, Henry Wisniewski, who runs a large Alzheimer's research laboratory at the New York State Institute for Basic Research in Developmental Disabilities on Staten Island, has come up with results suggesting that microglial cells produce it. "It looks like the microglial cells play a key role [in the formation of amyloid deposits]," Wisniewski says. If he's right, the net result could indeed be a vicious spiral of nerve cell destruction as microglial cells move in to clear out dying neurons and unleash still more damaging weapons, including the complement proteins and more β-amyloid.

The publication of the results of the indomethacin pilot study later this summer will attract attention to the role of inflammation in Alzheimer's. But Rogers already has at least one tangible indicator of the increasing seriousness with which his and McGeer's hypothesis is being taken. "My calendar this spring has been filled," he says, "with visits to drug companies."

–Jim Schnabel

Jim Schnabel is a free-lance writer based in Oxford, England.

ASTRONOMY

A New Way To Rev Up a Fast Pulsar

It's not easy to make a millisecond pulsar. First, you have to crush a star into a ball of neutrons just a few kilometers across and set this neutron star spinning rapidly, sending out lighthouse beams of radio waves that sweep across the sky with each revolution. And that's just for starters. Ordinary pulsars spin several times a second; to qualify as a millisecond pulsar, these unlikely objects have to spin hundreds of times faster. Now astronomers are finding to their surprise that, hard as the task is, there may be more than one way to do it.

Since the first millisecond pulsar was discovered 10 years ago, most astronomers have assumed that these objects start out as ordinary pulsars, which are thought to be the cinders left over from the stellar explosions known as supernovas. The theory holds that late in the life of a pulsar, when it is slowing down and its signal is weakening, it can be reborn as a millisecond pulsar when it gains mass and spin from a nearby star. But x-ray and radio observations are now hinting that many of the galaxy's millisecond pulsars may have skipped that earlier life. The recent results support a competing idea, that some millisecond pulsars are born when an ancient, compact star known as a white dwarf steals enough material from another star to collapse under its own weight into a fast-spinning neutron star. Says Yale University astrophysicist Charles Bailyn, an advocate of the white dwarf scenario, "This is the first qualitative advance in understanding the origin of millisecond pulsars over the last 5 years or so."

The idea that millisecond pulsars are resurrected ancient pulsars originated soon after the first one was discovered in 1982 by Donald Backer of the University of California, Berkeley, and his colleagues. Ordinary pulsars are born with powerful magnetic fields, which create a kind of friction that rapidly slows their rotation, but Backer's millisecond pulsar and others discovered soon afterward were losing speed quite slowly. That meant their magnetic fields had to be weak, which theorists took as a sign of extreme age—a few billion years or so. A neutron star that old, though, should be spinning much slower than run-of-the-mill pulsars, not hundreds of times faster.

The leading explanation for the paradox is that these pulsars were "recycled" when they drew in material from a close companion star. Because the companion star was whirling in orbit around the neutron star, the added material would have given the pulsar a hefty dose of additional spin. Indeed, astronomers think they've picked up direct evidence of this accretion process: x-ray emission from binary systems in which one star is orbiting an unseen companion, presumably a neutron star. Astronomers believe that the x-rays are given off as material from the first star rains down on the neutron star.

A few theorists, though, have insisted that there's a problem with this picture: There may not be enough of these so-called low mass x-ray binaries (LMXBs) to account for the burgeoning population of millisecond pulsars. As Bailyn puts it, "If each millisecond pulsar has once been a low-mass x-ray binary, then the birthrate of LMXBs had better be at least as great as that of millisecond pulsars." But while observers have so far discovered 10 LMXBs in the galaxy, and theorists estimate that about 100 more are still to be discovered, millisecond pulsars are far more plentiful.

In addition to the several dozen identified individually since Backer's discovery, Andrew Fruchter of Berkeley and Miller Goss of the National Radio Astronomy Observatory have detected the combined emissions from at least 75 millisecond pulsars in one dense knot of stars, or globular cluster. Fruchter estimates that there are a total of 500 to 2000 millisecond pulsars in the galaxy's other globular clusters and probably thousands more in its disk.

To Marco Tavani of Princeton University, the shortage of LMXBs may not be a problem. He suggests that observers have found so few of them because "their lifetimes are much shorter" than previously assumed, and therefore only a few are active at a given time. But Bailyn, together with Jonathan Grindlay of Harvard University and others, has been arguing that the shortfall points to the need for a more abundant source of millisecond pulsars—for example, white dwarfs that gain mass from a companion star and collapse. Like the proverbial ice skater drawing in his arms, the collapsing white dwarf would start to spin frenetically—but do so, according to calculations by Ganesh Chanmugam of Louisiana State University, without acquiring too strong a magnetic field.

But many astronomers had remained unconvinced. The scenario, says Tavani, is "on rather shaky ground." Some critics, like Frank Verbunt of the University of Utrecht in the Netherlands and Tavani, argue that adding new material onto a white dwarf might not precipitate a collapse. Instead it could lead to explosive bursts of nuclear burning called "novae," in which the white dwarf would lose more mass than it gains. If so, a white dwarf might never collect enough mass to become a neutron star.

Recent results from the x-ray satellite ROSAT, however, support the idea that material can be added to a white dwarf without causing a detonation. ROSAT investigators including Paul Hertz of the Naval Research Laboratory, who works with Grindlay and Bailyn, have spotted several x-ray sources that differ from LMXBs in giving off fainter, lower-energy radiation. Such "supersoft" x-ray sources, Edward van den Heuvel of the University of Amsterdam and his colleagues have proposed, are white dwarfs pulling material off companion stars. As in LMXBs, the infalling material emits the x-rays as it is compressed and heated—but because a white dwarf's gravity is weaker than a neutron star's, the heating is less intense and the x-rays less energetic.

KIM GORDON/PHOTO RESEARCHERS

Merger frenzy. White dwarfs colliding in the heart of dense globular clusters like this one, known as M22, may spawn millisecond pulsars.

And in last month's *Astrophysical Journal*, Kaiyou Chen of Los Alamos National Laboratory and Malvin Ruderman of Columbia University report evidence that this process can culminate in millisecond pulsars. They argue that a millisecond pulsar's origin should be apparent in its pattern of radio pulses. If an ancient neutron star is "spun up" in the traditional way, say Chen and Ruderman, the stress of the acceleration will tend to shift its crust until the two magnetic poles lie at exactly opposite points on its surface. But if the millisecond pulsar was born spinning fast, as in the white dwarf scenario, its poles wouldn't necessarily be symmetrical. Because a pulsar's radio waves originate at the two poles, the pattern of signals reaching Earth would be different in the two scenarios.

When Chen and Ruderman applied this test to a sample of observed millisecond pulsars, they found that some of them did show the asymmetric pulses predicted for the white-dwarf origin. What's more, the researchers discovered a spatial segregation: Most millisecond pulsars in globular clusters showed the asymmetry, while those in the disk of the galaxy showed the symmetry expected if they had been spun up late in life. "This is just what you'd expect if the millisecond pulsars in globular clusters were created through accretion-induced collapse," says a happy Bailyn.

As for why collapsing white dwarfs should be more common in globular clusters than in the rest of the galaxy, Chen and his Los Alamos colleague Peter Leonard offer an explanation in another paper, recently submitted to *Astrophysical Journal Letters*. They argue that the additional mass needed to trigger collapse could come not from material snatched from a binary companion but from a merger with a second white dwarf. The chance of a collision between two white dwarfs is thought to be slim in most of the galaxy. But in the dense core of a globular cluster, white dwarfs might tangle with each other more often.

Still, some researchers aren't sure the difference in the signals from millisecond pulsars really reflects differing origins. Among them is Princeton's Tavani, who says, "It's an interesting idea, but it's not 100% secure. Other interpretations for the differences [in magnetic fields] might be possible." Even though nature has no trouble turning out millisecond pulsars by the hundreds, it still seems to be a daunting job for Earthbound theorists.

–Ray Jayawardhana

Ray Jayawardhana is a science writer based in New Haven, Connecticut.

Additional Reading

Charles Bailyn and Jonathan Grindlay, "Neutron Stars and Millisecond Pulsars from Accretion Induced Collapse in Globular Clusters," *Astrophysical Journal* **353**, 159 (1990).

Kaiyou Chen and Peter Leonard, "Does the Coalescence of White Dwarfs Produce Millisecond Pulsars in Globular Clusters?," to appear in *Astrophysical Journal Letters*.

Kaiyou Chen and Malvin Ruderman, "Origin and Pulse Properties of Millisecond Pulsars," *Astrophysical Journal* **408**, 179 (1993).