MEETING BRIEFS

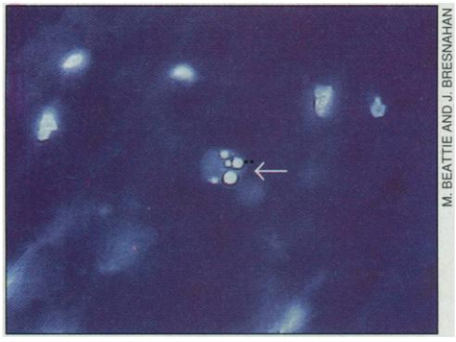
Neuroscience's Meeting of the Minds in Washington

WASHINGTON, D.C.—Nearly 25,000 neuroscientists gathered last week at the Washington Convention Center and in sessions at nearby hotels for what Society for Neuroscience president Pasco Rakic dubbed "the largest gathering of neuroscientists in the history of the world." Here are a few highlights from the meeting.

New View of Spinal Cord Injury

Every year, spinal cord injuries leave up to 15,000 people in the United States partly or totally paralyzed. The only treatment now is the steroid drug methylprednisolone, which can curb some of the damage if given within 8 hours of the injury. But many spinal cord patients are still left devastated. Research presented in Washington suggests a new strategy for reducing that toll.

In work done with rats, four teams, led by Michael Beattie and Jackie Bresnahan at Ohio State University College of Medicine in Columbus, Dennis Choi of Washington University in St. Louis, Russ Nockels and Michael Chopp at Henry Ford Hospital in Detroit, and Barry Festoff of the Veterans' Administration Medical Center in Kansas City, Kansas, focused on a wave of spinal-cell death that continues for up to 3 weeks after the injury. They found that the cells die not from damage done by the blow itself, but from programmed cell suicide (apoptosis). And they report hints that stopping that apoptosis could reduce the extent of paralysis.



M. BEATTIE AND J. BRESNAHAN

Slow death. Spinal cord cells die from apoptosis *(arrow)* for up to 3 weeks after injury.

Researchers had known that much of the cell death in spinal cord injury is delayed but didn't know why. But the four groups now provide "definite evidence" that apoptosis is key to that secondary injury, says Andrew Blight, who studies spinal cord injury at the University of North Carolina. The research also suggests "a reasonable chance," he says, that apoptosis blockers being developed for treatment of other conditions may help limit spinal cord injuries.

All four teams used a rat model designed by Wise Young at New York University to reflect the most common kind of spinal cord injury in humans, in which the cord is not severed but is deeply bruised from a fall or a blow. The rat studies show that the initial injury destroys some of the neuronal axons running down the cord. But those that survive the initial blow aren't out of danger—damage and cell death continue to spread following the injury. Among the cells that die are oligodendrocytes, nonneuronal cells that wrap axons in insulating layers of myelin. Without the oligodendrocytes, axons lose their myelin and are unable to conduct impulses. Until recently, says Blight, some researchers thought that all this additional damage was the result of the slow death of cells already injured by the original blow.

Now, it seems that it's not. Examining the spinal cords of rats at various times after injury, the researchers found signs that the cells were dying not from physical injury, but from the orderly process of apoptosis, in which cells chop up their chromosomes while keeping their membranes intact. These findings aren't confined to rats; Bresnahan found similar signs of apoptosis in damaged monkey spinal cord as well.

Many of the dying cells are the myelin-producing oligodendrocytes. Because oligodendrocytes seem to need contact with healthy axons to survive, Beattie suggests that the dying back of some of the axons during the original injury could be the trigger causing the oligodendrocytes to die; their death could then cause further axon demyelination.

Because the apoptosis continues for 3 weeks following spinal cord injury in rats, it may open a longer window of opportunity for therapies, says Nockels. Indeed, both the St. Louis and Detroit teams have evidence in rats that such interventions may work. Choi's group treated injured rats with the protein synthesis blocker cycloheximide, which prevents apoptosis, and got a 50% improvement in the animals' ability to use their hind legs after the injury. "This gives a glimpse of the potential functional benefit," says Choi. However, cycloheximide is too toxic for human use, so human trials must await other apoptosis blockers now under development.

Neurotrophic factors, which protect neurons and other cells from apoptotic death, may be an alternative. Nockels's team implanted cells making nerve growth factor or brain-derived neurotrophic factor directly into injured spinal cords, and found that the animals recovered faster than controls. They haven't yet shown whether this is due to the prevention of apoptosis, however.

Nor do researchers know whether an antiapoptotic drug would add to the effects of methylprednisolone, because its mode of action is uncertain. "It would be great to test the two together," says Blight. But the new cell-suicide findings are encouraging, say the researchers. Someday, predicts Festoff, "the acute treatment for spinal cord injury ... is going to be a syringe."

–Marcia Barinaga

Leptin: A Trigger for Puberty?

The protein famous for making fat mice thin, in part by signaling their brains that they've eaten enough, also seems to regulate an entirely different kind of appetite: the sex drive. Endocrinologist Jeffrey Flier of the Beth Israel Deaconess Medical Center in Boston presented evidence here that leptin—a protein that has sparked enormous interest as a possible obesity drug since its discovery 2 years ago—helps regulate sex hormone production. Indeed, it may even be the trigger for the onset of puberty.

If so, the discovery would help explain a variety of observations made over the years relating body fat content to sexual behavior and fertility. Scientists have known for years, for example, that ballet dancers, marathon runners, and others with low body fat have disrupted reproductive systems, as do people who are starving. Women stop ovulating, and testosterone levels fall in men. Because leptin is made and secreted by fat cells, the drop in production that occurs in very lean or starving people might account for these changes—an idea described as "very satisfying" by Rose Frisch, a population scientist at the Harvard School of Public Health in Boston who has studied the connection between fat and fertility for several decades.

The work also adds to growing evidence that leptin's function is not only to prevent weight gain, but also to help the body conserve energy during a famine by regulating the complex neuroendocrine system that governs metabolism and the energy-expensive reproductive system, says Arthur Campfield, who studies metabolic diseases at Hoffmann-La Roche in Nutley, New Jersey, and who

organized a symposium here on leptin and its effects on the body's balance of energy. "It's a fundamental hormone of nutrition and survival," he says. "That's really the dominant thing it's designed to do."

The first clues that leptin is involved in reproductive behavior came earlier this year when Flier and his colleagues found that the protein can blunt several starvation-induced hormonal changes in mice. Testosterone levels, for example, were more than twice as high in starved mice treated with leptin as in their saline-treated counterparts. The protein also prevented the usual delay in starved females' estrus cycles. (The results were published in the 18 July issue of *Nature*.)

In more recent work, the Flier team has evidence implicating the protein in induction of puberty in both mice and humans. In one experiment, the researchers measured leptin concentrations in the blood of eight boys taking part in a study of puberty. They found that the concentrations increased sharply—to two or three times the normal level—at the same time that testosterone first became measurable in the blood, just before puberty's first outward signs appeared.

Such correlations don't necessarily prove that leptin is inducing puberty. But another mouse experiment, in which Flier and his colleagues injected low levels of leptin into normal female mice from the time they were weaned, supports the idea. Mice usually reach sexual maturity about 40 days after birth, but the leptin-treated mice showed signs of sexual maturity about 3 days earlier, Flier says.

Still, many questions remain to be answered. Flier and his colleagues do not yet know, for example, how leptin modulates sex hormone production, although it's likely that the protein works through the brain region called the hypothalamus. At least one of the protein's receptors is abundant there, and the hypothalamus is known to regulate many hormone-producing glands through its effects on the pituitary, the body's so-called master gland.

Nor do they know what causes the prepubertal spike in blood leptin concentrations. Although Frisch's work has shown that puberty in human females is delayed if they are too lean, Flier says that the leptin spike happens without any sudden weight gain, and he suspects that another signal is involved. He says a similar effect is apparent in mice: Young animals produce a leptin spike at a time when they have relatively little body fat.

As Campfield puts it, "We're just now beginning to open up the black box and see how leptin regulates body fat." But with leptin now implicated in sex as well as obesity, the appetite for research on the protein will only sharpen.

–Gretchen Vogel

PLANETARY SCIENCE

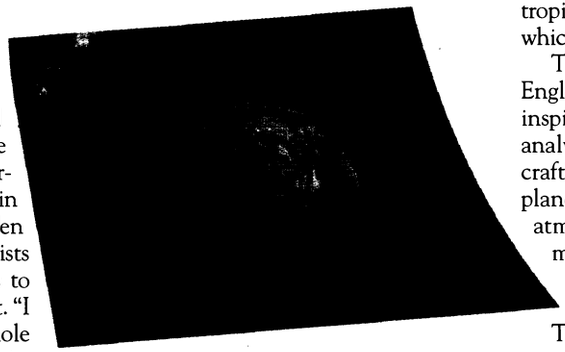
Found: Jupiter's Missing Water

TUCSON, ARIZONA—When the Galileo probe plunged into Jupiter's atmosphere last December, it left a deep mystery in its wake. Conventional theories of how the planets formed imply that this gas giant should have a few times as much water as the sun does, but the probe found a surprising dryness (*Science*, 2 February, p. 593, and 10 May, p. 814). Theorists began trotting out scenarios to explain how water could have been excluded from the forming planet or buried in its core. They can relax a bit now.

Additional analysis of data from the probe and new observations from the Galileo orbiter, presented here at last month's meeting of the American Astronomical Society's Division for Planetary Sciences (DPS), show that the abundance of water varies from place to place on Jupiter. And so most researchers now conclude, as some had suspected early on, that Jupiter's apparent dryness was just the probe's bad luck in falling into a dry spot. That shifts the burden of spinning new theories from cosmochemists to meteorologists, who are seeking ways to create deep dry spots on the gaseous planet. "I don't think anyone believes Jupiter as a whole is dry" anymore, says probe project scientist Richard Young of NASA's Ames Research Center in Mountain View, California. "Now it's more a question of how the [atmospheric] dynamics can make it dry at some places."

Three observations discussed at the DPS meeting have driven the shift from global to local Jovian dryness. It was obvious from the start that the probe had entered a "hot spot" (observable even from Earth), where parts of the atmosphere—wrung free of water during an earlier ascent—were descending. But researchers found it hard to imagine how such a downdraft could sink to the deep level reached by the probe, 150 kilometers beneath the cloud tops. Others argued that the deep dryness could be global. Now that some of the calibration problems induced by unexpectedly high temperatures in the probe have been resolved, however, the mass spectrometer has shown signs of wetter conditions in the deeper reaches of the atmosphere, implying that wetter atmosphere surrounded the hot spot.

Signs of moisture also turned up away from the probe site, in the form of high, thunderheadlike clouds imaged by the Galileo orbiter near the Great Red Spot (*Science*, 23 August, p. 1048). Planetary meteorologist Andrew Ingersoll of the imaging team and the California Institute of Technology (Caltech) noted at the meeting that the condensation of abundant water is probably the only process energetic enough to drive clouds so far above the planet's usual cloud deck. And the orbiter's near-infrared mapping spectrometer (NIMS) found that different hot spots have different amounts of water, again hinting that local processes, not global conditions, are responsible for the dry regions. "It's a dynamical problem," concludes NIMS team leader Robert Carlson of the Jet Propulsion Laboratory (JPL), "not a problem with the planet being dry to start with."



NASA/JPL

Signs of a storm. A tall thunderhead (white, *upper left*) in this false-color image of the Great Red Spot suggests abundant water on Jupiter.

Responding to the call, planetary meteorologists are now coming forward with ways to explain Jupiter's deep patches of aridity. Ingersoll and Adam Showman, also of Caltech, suggest that the dry Jovian downdrafts are so strong that they plunge deeper than their naturally buoyant level, just as updrafts in Earth's tropics sometimes overshoot the altitude to which their buoyancy should carry them.

Tristan Guillot of Reading University in England has a different slant on that idea, inspired by Uranus and Neptune. He has reanalyzed distortions in the Voyager 2 spacecraft's radio signal as it passed behind those planets in the 1980s, probing deep into their atmospheres. Tracing the abundance of methane rather than water, he finds signs that Neptune's atmosphere in particular is also "dry" to a surprising depth.

The mechanism of deep drying may be the same on all three planets, Guillot speculates: intense upwelling and downwelling, driven by the deep convection that carries heat outward from the planets' interiors. Such drying would be pervasive over large parts of the planet, not just at a few hot spots. For now, Young is reserving judgment: "At this point, I don't think we know [what's going on]." Perhaps not, but at least researchers may find the answers today, in the dynamics of Jupiter's swirling clouds, rather than in the long-ago chaos of its formation.

–Richard A. Kerr