tional investment," he says.

As part of the budget allocation, the government also announced a raft of measures to help improve career prospects for university researchers. This year it increased the minimum annual grant for Ph.D. students by $1600 to $10,500—the first increase above inflation for 30 years. And now the number of fellowships awarded by the Royal Society will be increased from 265 to more than 300. The increased research council budgets will also mean that university-based researchers on council grants will be able to hire more graduate and postdoctoral staff, and the councils' own labs will also be able to create new positions.

Even the lobby group Save British Science, a longtime critic of government funding policy set up during the previous Conservative government, could find little to complain about. Says lobby chair Richard Joyner, dean of research at Nottingham Trent University: "I'm very pleased to see that everybody has got something." —NIGEL WILLIAMS

AGING RESEARCH

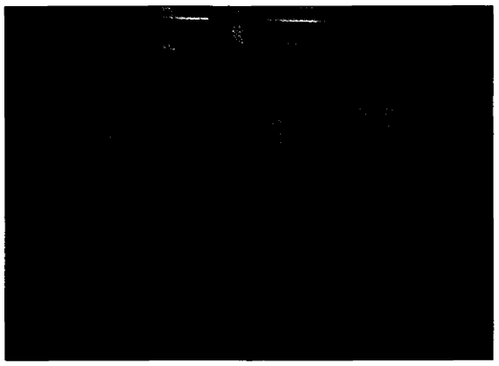
Low-Calorie Diets May Slow Monkeys' Aging

Scientists are edging closer to proving in primates what's been demonstrated dozens of times in rodents since the 1930s: Sharply reducing caloric intake can slow the process of aging to a crawl.

At a Society of Toxicology meeting 2 weeks ago in Reston, Virginia, three groups presented data showing that rhesus monkeys fed severely calorie-restricted diets show fewer signs of diseases associated with advancing age, including diabetes, heart disease, and cancer, than their comfortably full—and in some cases comparably lean—counterparts. Because most of the hungry monkeys are only now entering middle age, it's too early to tell whether the low-calorie diets will significantly extend their life-spans. But one of the studies provided a tantalizing hint: Mortality due to disease among the calorie-restricted monkeys was slightly lower than among the controls.

Even if monkeys do live longer on low-calorie diets, it doesn't necessarily follow that humans would experience similar benefits—or that they would find such diets acceptable. But researchers hope that these animals might provide clues to why calorie restriction is beneficial—information that could point to strategies and medications for delaying aging in humans.

The three groups reporting their results at the meeting—which were led by Mark Lane at the National Institute on Aging (NIA), Richard Weindruch at the University of Wisconsin, Madison, and Barbara Hansen at the University of Maryland, Baltimore—kept the animals on tight rations but well above starvation levels. The Wisconsin and the NIA teams provided the test animals with 30% fewer calories than the controls (while enhancing their diets with a vitamin and mineral supplement), while Hansen tailored the monkeys' food intake to prevent them from putting on more pounds than they carried in young adulthood.



Hungry but healthy. Monkeys eating sharply restricted diets (right) may live longer than well-fed controls.

All three groups found that in nearly every system tested, the calorie-restricted (CR) animals were better off than the controls. All recorded lower blood lipids and blood pressure, enhanced insulin sensitivity, and a lower incidence of diabetes in calorie-restricted monkeys. The Wisconsin group also found less spinal arthritis, while Lane's team saw fewer cancer cases and a slightly lower mortality rate due to diabetes and cardiovascular disease. One of the 120 animals on the diet died, compared to five among the 120 controls. "[The] major message from the monkeys is that 99.9% of those markers that we have examined in the monkeys behave exactly as they do in rodents," says Lane.

What's more, the severe calorie reduction seems to produce few adverse effects. Lane's group, which began caloric restriction in young animals, saw the only potential problem: delayed sexual and skeletal maturity. None of the primates have been bred, however, so no one knows whether their reproductive capabilities are affected. And although all three groups acknowledged that their animals were regularly hungry—wolfing down food more quickly than controls, or becoming excited if accidentally given excessive food—none found that the added stress affected behavior. Controls and CR monkeys were equally energetic, social, and nonaggressive, and a weeklong videotape of Lane's animals showed no measurable differences between the two groups.

Why caloric restriction so dramatically improves the functioning of organ systems remains under debate. Certain changes, like the reduced incidence of diabetes, might simply be a benefit of leanness, as obesity predisposes to the disease in nonhuman primates as well as in most humans. Others are more puzzling, however.

One possibility, Weindruch says, is that restricting food consumption reduces the production of tissue-damaging oxygen free radicals that are a byproduct of food metabolism. He has shown in mice that such oxidative damage leads to muscle atrophy, producing the frailty common in old age.

But reducing oxidative damage is only one way calorie restriction might work. "The problem with [caloric restriction] is that it fits any of the theories of aging," says Roy Walford, a professor of pathology at the University of California, Los Angeles, and a pioneer in the field. "[It] increases DNA repair, regulates glucose insulin, decreases free radical damage, preserves the immune system."

The primate studies haven't gone on long enough to determine whether caloric restriction will result in the kind of increases in life-span seen in near-starving rodents, which live up to 40% longer than controls. Rhesus monkeys can live up to about age 40 in the lab, whereas the test animals are still in their mid-20s. The primate data are "very tantalizing preliminary results," says Lane. "But [I'm] not at the point where I'm willing to stand up and wave the flag and say it works."

If further work confirms that caloric restriction pays off in extended primate life-spans, though, and researchers can pin down the reasons why, aging experts hope to tap into something that, until now, has been restricted to the realm of fiction—controlling the process of aging. —JENNIFER COUZIN

NEUROBIOLOGY

New Leads to Brain Neuron Regeneration

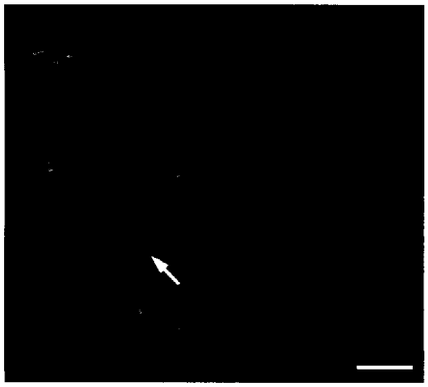
Neurobiologists have long considered the neurons in the adult brain to be like a precious nest egg: a legacy that dwindles with time and illness and is difficult if not impossible to rebuild. Two sets of findings published this week raise hopes that this principle could one day be overturned. In one, research teams at Harvard and the National Institute of Neurological Disorders and Stroke (NINDS) independently isolated what appear to be the first human cells that can differentiate into all the cell types found in the brain—so-called neural stem cells. In the other, a team based in California and Sweden found a small area of the human brain that produces new neurons into old age.

The discoveries aren't biologically surprising, because both neural stem cells and

CREDIT: JOSEPH KEMNITZ, JON RAMSEY

the birth of neurons in adult brains have been seen in other mammals. But identifying them in humans was a demonstration that could be critical to future therapies for diseases such as Parkinson's or Alzheimer's. The stem cell results, reported in the November issue of *Nature Biotechnology*, "provide proof of principle that you can do this with human cells, and that is a necessary step on the way to using these cells in the treatment of human diseases," says developmental neurobiologist David Anderson of the California Institute of Technology in Pasadena. And the discovery of neuron growth, reported in *Nature Medicine*, raises an even more enticing—although distant—prospect: inducing patients' own brain cells to regenerate neurons lost to disease.

The two teams that discovered the stem cells, led by Evan Snyder at Harvard Medical School in Boston and by Ronald McKay of the NINDS, both began by culturing cells from the brains of aborted human fetuses. The first clue that the cultures contained stem cells was the fact that some of the cells would differentiate into the three main types of brain cells: neurons and two types of support cells called glia. The true test of a stem cell, however, is to show that one cell can give rise to all the different cell types of a tissue. (For reports on stem cells from an earlier stage of development, which can differentiate into a wider range of tissues, see pp. 1014 and 1145.)



Newborns. BrdU (green) integrated into the DNA marks new cells, which stain as neurons (red) rather than glia (blue).

To show that they had neural stem cells, Snyder's team cloned a single cell and then showed that cells from that cloned culture could differentiate into glia and a variety of neuronal types when they were put into developing mouse brains. McKay's group didn't develop clones of identical cells. But they did transplant sets of cells that appeared identical into the brains of fetal rats in utero and found that the cells joined the rats' own neurons in forming various kinds of brain tissue. While acknowledging that there is much more research to be done, Snyder says he hopes the field will be ready "to start applying this to human diseases within 5 years."

The prospect of coaxing the brain to heal itself is even more distant. But thanks to work by Fred Gage of the Salk Institute in San Diego and Peter Eriksson and his colleagues at the Sahlgrenska University Hospital in Göteborg, Sweden, it is no longer considered impossible.

For years neurobiologists thought that no new human brain neurons are generated after birth. That view was bolstered in the 1980s by work in which Pasko Rakic's team at Yale University found no evidence that neurons are dividing in the brains of rhesus monkeys. However, researchers later turned up evidence of new brain neurons in adult rodents, tree shrews, and marmoset monkeys. But no one had come up with a way to perform the absolute test—looking in human brains.

To answer the question once and for all, Gage, Eriksson, and their colleagues took advantage of a cancer study in Sweden. Patients had been given a marker chemical called bromodeoxyuridine (BrdU), which is incorporated into the DNA of dividing cells, to follow the growth of their tumors. After five of those patients died, the scientists examined samples of their brain tissue. They found BrdU-labeled neurons in the dentate gyrus, a small part of the brain area called the hippocampus, which is involved in forming memories. This was a telltale sign that those cells had been recently formed by the division of precursor cells.

This means, says Gage, that "neurogenesis does not stop phylogenetically at [marmosets]" and that human brains do replace neurons. In fact, Rakic says that, with techniques similar to Gage's, his lab has filled in the missing link between humans and marmosets by finding evidence of new neurons in the dentate gyrus of rhesus monkeys. They will present the finding at the annual meeting of the Society for Neuroscience in Los Angeles next week.

Rakic and Gage caution that the practical significance of the discovery is unclear. The dentate gyrus is just one small brain area, says Rakic, and "the principle [of no new neurons] still applies for most structures of the brain." Gage adds, "We don't have any evidence that these cells are hooked up in any way" to functioning neural networks.

But the finding could mean that researchers might someday learn how to encourage regeneration in other parts of the brain, such as areas hit by neurodegenerative disorders. That's a tall order, but it is a concept that people "weren't even thinking about" before this finding, says Gage.

—MARCIA BARINAGA

CREDITS: (TOP) ERIKSSON *ET AL.*, *NATURE MEDICINE* 4, 11 (NOVEMBER 1998); (BOTTOM) S. STRICKLAND/NATURESCAPES

ScienceScope

TIMING TROUBLES AT NASA

As in comedy, timing can be everything when it comes to setting priorities for space science. Last week, members of a NASA science advisory panel said they are worried that the agency's timetable for an upcoming 3-year strategic plan doesn't leave enough time for input from space scientists participating in a similar blue-ribbon study being conducted by the National Academy of Sciences. Both efforts are intended to influence the direction of space studies in the next decade.

Researchers would like to see NASA push back the deadline for its report, which is due in June 2000, in order to influence congressional debate on the agency's 2001 budget. The academy's review, done every 10 years, is set to begin in January and also finish in mid-2000. "If the two reports are perceived as saying different things," says Dan Lester of the University of Texas, Austin, "the science community could shoot itself in the foot."

EPA INVITES COMMENT ON PESTICIDE POLICIES

Chemical industry officials have won the chance to comment on key pesticide science policies that will guide enforcement of a 1996 food safety law—despite complaints by environmental advocates that what's needed is action, not more words.

Last week, the Environmental Protection Agency (EPA) released a plan for receiving public comments over the next year on nine key technical issues raised by the law. They range from how to statistically analyze human exposure to pesticides to how to deal with chemical residues on food that may be dangerous but are not measurable with existing equipment.

Industry representatives serving on an EPA advisory panel successfully pushed for the chance to comment on what they see as an overly strict interpretation of the policies, which will shape enforcement of the law. But one environmentalist says some companies are just trying to slow things down. "EPA has received more than enough information on these issues," says Ken Cook of the Environmental Working Group. "It should be regulating instead of issuing documents."

Contributors: Christie Aschwanden, Gretchen Vogel, David Malakoff