September triggered a campaign by scientists and members of Pasadena's Planetary Society to boost congressional interest in the once-obscure mission. It appears to be having the desired effect: On 28 October, Representative James Walsh (R–NY), who chairs the House panel that approves NASA's budget, noted that "Pluto remains the only planet in the solar system" unvisited by spacecraft. He also said that the mission would provide data on the small bodies beyond Pluto that populate the Kuiper belt. Walsh has asked NASA for an explanation for the announced delay to "clear up any confusion on the part of our members."

That pressure has put NASA managers in a delicate position. Agency officials say they would like to keep Pluto on track despite rising costs and an uncertain budget. But they don't want to get into a fight with the White House over the Europa mission. Proponents hope to tip the balance in favor of the outermost planet without upsetting those more focused on Europa. "NASA is going to see it will be greatly to their advantage to restart [Pluto] expeditiously," says Stern. "They missed a bet—this mission is a keeper."

–ANDREW LAWLER

NEUROBIOLOGY

Heretical View of Visual Development

In the 1960s, two Harvard neurobiologists turned thinking about brain development on its head, showing that experience itself could alter the structure of the brain as it continues to mature after birth. David Hubel and Torsten Wiesel found in monkeys and cats that seeing out of both eyes is necessary for the normal arrangement of so-called ocular dominance columns—neat columns of brain cells that respond to visual activity from one eye or the other. This work led to the deeply rooted belief that the columns form as a result of visual activity—a belief now being called into question.

In work described on page 1321, Duke University neuroscientists Justin Crowley and Lawrence Katz report that ocular dominance columns in ferrets appear long before the columns can be modified by visual experience. Even more heretical, they present data suggesting that neural activity from the eyes has little influence over the formation of the columns. They propose instead that innate molecules that guide growing axons to their locations in the developing brain may be primarily responsible for building these columns.

"It's a very beautiful study," says Harvard neuroscientist Carla Shatz. "There's no question that they showed that ocular dominance columns form earlier than we thought." But Shatz and others contest the conclusion that neural activity is not required for constructing the columns, arguing that there are other explanations for the researchers' findings. "I'm agnostic about that [conclusion]," Shatz adds.

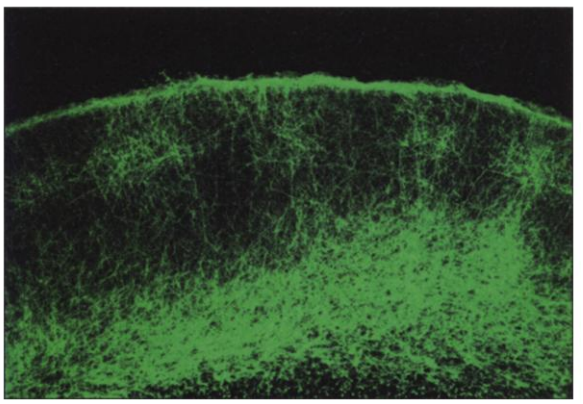
If the Duke team's conclusions are correct, however, they may once again drastically alter the way scientists view how the brain matures. What's more, if the purported molecular signals that shape sophisticated visual structures can be found, they may provide a new handle on the cause of myriad visual or other brain-related birth defects that now go unexplained.

But those are big "ifs." For years, research confirmed and extended Hubel and Wiesel's findings. In 1978, three of their Harvard protégés, Simon Levay, Michael Stryker, and Shatz, showed that in cats, the ocular dominance columns don't appear in the visual cortex, a region near the back of the brain, until 3 weeks after birth. That coincides exactly with the "critical period" in the animals, the time when Hubel and Wiesel had found that shutting one eye could disrupt the structure of the columns. So the scientists concluded that visual stimulation from both eyes is essential for the columns' initial formation.

But later work cast doubt on this analysis. Biologists showed several years ago, for example, that the columns are present at birth in monkeys and so must form before the critical period when they could be modified by visual experience. Still, researchers refused to retreat entirely from the idea that neural activity is essential, arguing that the spontaneous firing of neurons from the retina before the eyes open shapes the columns.

Three years ago, Crowley and Katz set out to test this hypothesis in ferrets. These animals were ideal because their nervous systems at birth are 3 weeks less developed than those of cats, enabling the detection of earlier developmental events. In work published last year, the researchers removed both eyes from newborn ferrets in an attempt to cut off any neural activity from the eyes that might influence the development of the columns.

Next the researchers wanted to find out whether that operation had in fact blocked column formation. When the animals reached adulthood, the researchers injected a tracer into eye-specific cells in the lateral geniculate nucleus (LGN) of the brain, through which visual signals travel en route to the cortex. Once the tracer traveled to the cortex, it revealed neatly ordered ocular dominance columns. So, says Crowley, "we concluded that retinal activity could not be as important as we thought it was" for forming the columns.



Premature? The micrograph shows ocular dominance columns in the ferret visual cortex before the onset of the critical period.

But still, questions remained. Crowley and Katz wondered whether they had removed the eyes early enough—that is, before the columns had formed. So in the current study, they used their tracer technique to time the formation of the columns. They found that the columns were not present at birth but appeared as early as 16 days later, which is equivalent to a week before birth in cats. "In pushing the day back," says Stryker, now at the University of California, San Francisco, "it becomes even clearer that the formation of the ocular dominance columns precedes the onset of plasticity" in the critical period.

But even though lack of input from both eyes hadn't affected the columns, skeptics argued that it might take an imbalance in input—for instance, having signals from one eye but not the other—to disrupt ocular dominance formation, as it does later during the critical period. To counter such claims, Katz and Crowley removed just one eye from each of six ferrets at an age when

CREDIT: J. CROWLEY AND L. KATZ

the LGN axons had linked up with the cortex but before the columns had formed. The doubters were wrong again: These ferrets still formed normal-looking ocular dominance columns.

Even that finding has not closed the case against neural activity, however. Shatz points out that the Duke scientists did not check to see whether the columns they saw after they removed one eye alternated in responding to either the right or left eye as they should. Thus, it could be—as Shatz has found in the past in cats—that removing one eye altered the visual system such that seemingly normal ocular dominance columns formed, but they all responded to the remaining eye. And Stryker points out that the study did not rule out the very real possibility that activity in the brain—say, from the LGN—is necessary for column formation even if that from the eye isn't.

Katz concedes that these arguments are valid, although he doesn't believe they explain his findings. He's now aiming to identify the molecular signals that he thinks guide the formation of ocular dominance columns. Says Katz: "My gut feeling is that we need to look in a different direction."

–INGRID WICKELGREN

NEUROSCIENCE

An Antibiotic to Treat Alzheimer's?

NEW ORLEANS—An antibiotic once used to treat traveler's diarrhea might battle Alzheimer's disease as well, researchers announced here last week at the Society for Neuroscience's annual meeting. The drug dissolves Alzheimer's-like plaques in mouse brains, apparently by trapping the copper and zinc that stud these deposits. A clinical trial to test whether the drug helps people with Alzheimer's is already under way.

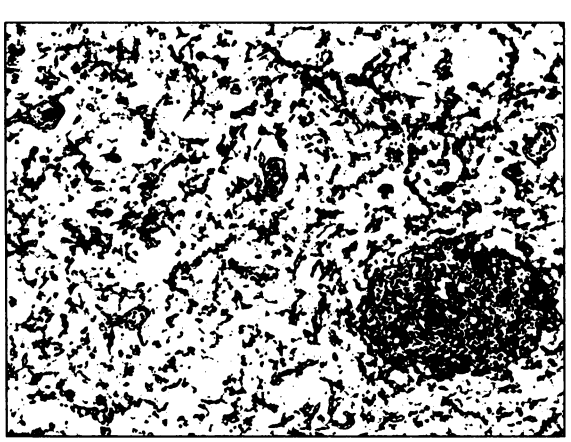
Deposits called amyloid plaques riddle the brains of people with the disease—who now number about 4 million in the United States and may reach 14 million by 2050. The plaques' primary ingredient is a protein called β amyloid (Aβ) that occurs normally in the body and doesn't appear dangerous in its soluble form. "We're not trying to stop [Aβ] from being produced—we're trying to stop it from being accumulated," says Ashley Bush of Massachusetts General Hospital in Boston.

To do so, Bush has been studying the effects of copper and zinc on Aβ. About a decade ago, he found that these metals allow enzymes to cut Aβ from a larger protein; he later discovered that they influence the properties of Aβ itself. Adding zinc to the protein in a test tube, for instance, can cause clumps of Aβ to form, and compounds that bind to copper and zinc can dissolve amyloid plaques in postmortem brain tissue from people who died with Alzheimer's disease.

In search of a candidate drug, Bush's team screened dozens of antibiotics and anti-inflammatory drugs known to bind metals. An antibiotic called clioquinol proved the most potent, efficiently dissolving plaques in postmortem tissues and reducing amyloid's ability to clump together. To test whether clioquinol could clear up amyloid plaques in the brain of a living animal, the team gave the drug to young mice engineered to develop Alzheimer's-like deposits. The drug appeared to inhibit plaques from forming: The animals developed fewer plaques overall, and some 30% developed no detectable plaques. In a second study, the drug appeared to clear up plaques in mice old enough to have developed substantial deposits. Those given the drug for 9 weeks had 50% less amyloid deposited in their brains than untreated animals had.

The mouse studies are "very impressive," says Alzheimer's researcher David Morgan of the University of South Florida in Tampa, showing "a dramatic reduction [of plaques] in a very short time." Other approaches, including vaccinating mice against Aβ, also clear plaques from mouse brains (*Science*, 9 July 1999, p. 175).

The Food and Drug Administration approved clioquinol decades ago as an antibiotic. The drug was used for about 500 million patient days, Bush says, but was pulled from the market after a few people developed an acute vitamin B-12 deficiency while taking the drug. Although the B-12 deficiency can be addressed with supplements, Morgan cautions that the drug has not been tested for the long-term use necessary to help people with Alzheimer's.



CREDITS: (TOP TO BOTTOM) FRED CHARTRAND/AP; SIMON FRASER/PHOTO RESEARCHERS

Dissolved. Extracting metal shrinks amyloid plaques (in purple and blue).

ScienceScope

On the Stump Canadian scientists are being promised wheelbarrows of cash if the governing Liberals are returned to office in the 27 November election. Prime Minister Jean Chrétien (below) last month unveiled a campaign platform that calls for doubling annual federal research spending to $3.95 billion within a decade.

Hoping to put more distance between his Liberals and the right-wing Alliance Party, Chrétien promised to make Canada "a hotbed of research and investment." In particular, the Liberals call for boosting annual research outlays by at least $670 million within 4 years. The Canadian Institutes of Health Research would get an unspecified "major increase," while a quarter of the new monies are pegged for environmental research on toxins and children's health; clean air; and soil, water, and food safety. The remainder would be disbursed among the granting councils and in-house labs like those at the National Research Council.

The opposition Alliance also vows to increase granting council budgets by an unspecified amount and would appoint a "Chief Scientist of Canada to coordinate science activities in all government departments and ensure that science, not politics, prevails."

Mad About the Cow Concern about a surge of "mad cow disease" in France has proved a boon to the country's prion researchers. Prime Minister Lionel Jospin announced this week that the government will triple funding for research into prions, the abnormal proteins that are suspected of causing mad cow disease and its fatal human version, vCJD.

The move came after the agriculture ministry reported that there have been 80 cases of mad cow disease in France so far this year. That is equal to the number of cases over the previous 11 years, but still far short of the 170,000 cases recorded in the United Kingdom since 1988. And although France has documented just three human cases of vCJD, compared to 85 in the United Kingdom, news of the surge sparked what the press has called "a national psychosis." Jospin's package to calm fears, according to the newspaper *Le Monde*, includes an indefinite ban on giving livestock feed that contains animal bone and tissue, which is believed to spread the disease, and boosting the prion research budget to $27.5 million, starting next year.