progression of Alzheimer's symptoms in patients with moderately severe disease.

Neil Buckholtz, who manages the Alzheimer's drug development program at the National Institute on Aging in Bethesda, Maryland, says the results are interesting because "there's nothing else I know of that's worked for that population." What's more, he notes, the work suggests a new strategy for combating Alzheimer's.

The only other Alzheimer's drugs currently approved in the United States, which are directed at mild to moderate disease, act by bolstering the function of a group of neurons that are lost in the patients' brains, contributing to their mental decline. These neurons use the chemical acetylcholine to transmit their signals. In contrast, memantine turns down the activity of the so-called NMDA receptor, which responds to the neurotransmitter glutamate and whose overactivity may lead to neuronal damage in Alzheimer's.

In Germany, memantine has been approved for treating dementias for 10 years, but the study described by Reisberg—a phase III trial designed to test the drug's efficacy—is the first conducted in the United States. It included 252 Alzheimer's patients, who were treated at 32 clinical centers throughout the country. All had reached the stage when they begin to lose the ability to perform such basic daily functions as dressing and bathing and become incontinent. At the end of this stage, Reisberg says, family caregivers often find that they have to institutionalize the patients.

For the trial, the patients were divided into two groups, one of which was given memantine while the other received an inactive placebo. A variety of behavioral and intellectual assessments showed that all the patients declined over the 28-week course of the trial, but the decline was significantly slower in those taking the drug. "There was less deterioration. That makes a big difference in the burden of care," Reisberg says. He also notes that memantine seems to be well tolerated, causing few, if any, side effects. "Manipulation of the NMDA receptor system seems to be a promising target for treating Alzheimer's disease," Reisberg concludes.

Recent clinical trials in Europe, including one reported in the February 1999 issue of the *International Journal of Geriatric Psychiatry* by researchers in Latvia and at Sweden's Karolinska Institute, also bolster the case that memantine may be effective for slowing progression of dementias. Buoyed by these results, Merz & Co. of Frankfurt, Germany, which produces the drug, has entered into a partnership with Forrest Labs of New York to pursue plans for marketing memantine in this country—provided the U.S. Food and Drug Administration approves it.

–JEAN MARX

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ANIMAL RESEARCH

Activists Win Big on Rodent, Bird Rules

Animal-rights activists may have landed a knockout blow in their decade-old fight to force the U.S. government to regulate the use of laboratory mice, rats, and birds. Some research groups worry that the impact could send academic and industrial labs reeling.

A federal judge last month ruled that the activists have the legal right to challenge U.S. Department of Agriculture (USDA) rules that exempt the vast majority of research animals from federal regulation. Although the department has yet to respond, observers say that the ruling almost guarantees that the agency will extend regulations governing animal handling and housing to thousands of academic and industry laboratories that work with rodents and birds. Those new rules, say animal-care experts, could impose costly new requirements on labs that don't meet standards set by the private Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC). And even AAALAC-accredited institutions worry that USDA might design its rules in ways that would require new equipment and record keeping.

Rat rules. Researchers using birds and rodents, such as this rat, could face increased regulation.

The lawsuit was filed last year by a coalition led by the Alternatives Research & Development Foundation (ARDF) of Eden Prairie, Minnesota (*Science*, 5 February 1999, p. 767). It seeks to reverse a 1972 USDA decision to leave mice, rats, and birds—which account for more than 95% of all research animals—off a list of laboratory animals regulated under the 1966 Animal Welfare Act (AWA). USDA has claimed discretion to decide which animals are exempt from regulations that require researchers to open their facilities to annual surprise inspections and to consider alternatives when designing experiments.

Animal-rights groups won an earlier round when a federal court ruled in 1994 that USDA's claim was "strained and unlikely." But an appeals court made that decision moot by ruling that the groups had no legal "standing" to sue because they couldn't demonstrate that their members were directly harmed by the regulations.

ARDF took a different tack. One of the parties to the case was Kristine Gauz, an undergraduate psychology student at Beaver College in Glenside, Pennsylvania, who claimed to have suffered "aesthetic and emotional injury" from working with laboratory rats that she says received inadequate housing and veterinary care. In a 21 June ruling, U.S. District Judge Ellen Segal Huvelle concluded that Gauz has standing. "A researcher who witnesses the mistreatment of rats in her lab must have standing," Huvelle wrote, adding that USDA does not have "unreviewable discretion to exclude birds, rats, and mice from the AWA's protection."

USDA officials won't comment on the litigation, but agency sources say they expect Secretary Dan Glickman to decide within a month whether to throw in the towel. The betting is that he'll try to negotiate a timetable for phasing in regulation of the animals. "I'd be surprised if they shed any more blood on this," says John Miller, executive director for AAALAC in Rockville, Maryland. "It is clear to everyone that USDA cannot possibly win," crows ARDF chief John McArdle.

Writing and implementing any new rules could take years, however. And there is also the question of money. Miller predicts that the added oversight of thousands of small colleges, start-up biotech firms, and backyard bird breeders might require doubling USDA's current $10 million animal-care budget and staff of 70 inspectors.

Congress may be amenable to such a request. Last year, a coalition of animal-rights and animal-care groups won a $1 million increase for USDA's inspection budget, and this year they are closing in on a $2 million boost. The need for more funds, Miller notes, unites "the otherwise warring factions."

–DAVID MALAKOFF