

# *NIH agency devotes millions to* **alzheimer's RESEARCH**



## **New initiative could shorten time frames, costs for clinical trials** | BY STEPHEN BARLAS

**T**he death of former President Ronald Reagan has focused new attention on Alzheimer's research, which is flagging, except for a new imaging clinical trial expected to begin this fall.

The National Institute on Aging (NIA), which is the NIH's leading funder of Alzheimer's clinical research, has set aside \$40 million over five years for its Neuroimaging Initiative (NI) starting in fiscal 2005, which begins on Oct. 1. Susan Molchan, MD, program director of Alzheimer's research at the NIA, said the Neuroimaging Initiative funds have been "set aside," meaning they cannot be diminished if NIA funding from Congress falls short of what the Institute expected.

In addition, the NIA hopes to add another \$20 million to the NI. Those would be funds donated by pharmaceutical and medical device companies, including GE.

### **A window into the brain**

The NI is a high priority because it presents the possibility of shortening the current time frames and costs for Alzheimer's clinical trials. Instead of using behavioral endpoints, as is the common practice with Alzheimer's clinical trials, the NI will use neuroimaging techniques such as positron emission tomography (PET) and magnetic resonance (MR) imaging to chart changes in the brain, to assess biological markers for Alzheimer's and to see whether the disease is mitigated by prospective treatments.

For example, drug companies will find out whether prospective drugs reduce the amount of amyloid in the brain. Amyloid is a toxic protein closely associated with plaque and tangle development, cell death and loss of connections between neurons, all of them

linked to Alzheimer's.

"Powerful imaging techniques, including PET and MRI, are opening a window into the brain, allowing us to visualize not only anatomical structures but also functional processes and activities at the molecular level," said Richard Hodes, director of the NIA. "Visualization of brain structures and activities may also enable us to identify people at risk of developing the disease even decades before the onset of symptoms."

In a recent study, investigators used PET to examine the brains of asymptomatic young adults (ages 20-39) who were carriers of the APOE-e4 gene, a common susceptibility gene for late-onset Alzheimer's. Middle-aged carriers of this gene are known to have abnormally low rates of metabolism in the same brain regions as patients with Alzheimer's. In this study, the investigators found the same brain abnormalities in the younger carriers of the gene.

The precise link between the APOE-e4 gene, the altered metabolism, and Alzheimer's remains unknown, and more research is needed on this provocative finding.

### **Funding constraints**

Hodes testified about the NI before the Senate Health, Education, Labor and Pensions Committee on May 11, a month before President Reagan died. The hearings were held at the initiative of Sens. Kit Bond (R-Mo.) and Barbara Mikulski (D-Md.), the chairman and ranking Democrat on the Aging subcommittee.

Also at the hearings was Stephen McConnell, senior vice president for advocacy and public policy at the Alzheimer's Association, who decried ebbing funding

for Alzheimer's at the NIA.

In the current fiscal 2004, for example, the NIA budget for Alzheimer's research is \$518 million, making it the Bigfoot among NIH agencies in that area.

McConnell said the NIA is already holding back previously promised funding in response to a smaller-than-expected 2004 budget and an expectation that the 2005 budget won't be much better.

He said that the NIA success rate—the proportion of applications for research grants which are funded—isn't expected to exceed 15 percent in 2004, considerably below the Institute's recent historic level of 25 percent. "They are expecting each grant to be cut by 18 percent, too," he added.

Dr. Molchan emphasized that the \$40 million set aside for the NI starting in fiscal 2005 is sacrosanct, but she conceded that continuing NIA budget shortfalls would hinder any efforts to expand the NI with "follow on" projects.

Alzheimer's funding constraints would quickly fade away if Congress passes the Ronald Reagan Alzheimer's Breaththrough Act of 2004, which Sen. Mikulski introduced days after the former president passed away. The bill would double funding for Alzheimer's research at the NIH.

However, even if the bill did pass—and that is far from certain—it would be up to the Appropriations Committees in both houses to actually approve the budget increase which, in the current federal deficit-heavy climate, is very unlikely to happen. ■

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