

## US Alzheimer's disease researchers feel the pinch

In the USA, public and political awareness is growing about the importance of funding research into Alzheimer's disease, and yet the National Institute on Aging is supporting fewer and fewer research grant applications. Ruth Williams asks why, and what can be done.

For the open letter from NIA see <http://www.nia.nih.gov/GrantsAndTraining/Hodes2010-10-25.htm>

Gary Landreth, Director of the Alzheimer Research Laboratory, Case Western Reserve University, Cleveland, OH, USA, is in despair. Come June 1, 2011, he will be losing four of his laboratory staff when a grant from the National Institute on Aging (NIA) he has held for 15 years runs out. "My previous experience with the NIA has been fantastic. They've funded productive research programmes and kept me alive for 15–20 years. My more recent experience has been absolutely horrible." Although Landreth's application for the grant's renewal received a favourable score from NIA reviewers, "with the NIA's payline now in single digits, it won't pay", he explains. "It means I can no longer work on the area for which I am best known. That is psychologically devastating."

The NIA's payline—a percentile-based funding cutoff to select the top-ranking applications—has been steadily dropping over the years. It was at 14.6% in 2007, 14.2% by 2008, 11.6% by 2009, and then took a dramatic plunge in 2010 to 8%. Simply put, this means that the percentage of research grant applications funded by the NIA in 2010 was lower than ever. "It was a bad year", concedes Robin Barr, head of the NIA's Division of Extramural Activities. "We had the tightest funding line across the entire NIH."

The payline is just a guide. A recent programme project grant renewal from Stephen Ginsberg (Nathan Kline Institute and New York University Langone Medical Center, Orangeburg, NY, USA) and others scored within the top 3%. "When you score in the third percentile you usually think that it is funded", says Ginsberg, "so it was quite a shock the day before Christmas when we found out that it wasn't." Ginsberg, like Landreth, is losing staff.

"So far I've had to let go one person and another two are dangling", he says.

With the likelihood that even strong applications will be turned down, researchers are looking elsewhere for funds, and, to do so, are changing their research focus. Some are planning dramatic changes. Landreth says he has decided he must "get out of Alzheimer's research as fast as I can in order to stay alive". Ginsberg has chosen to focus more on his schizophrenia and Down's syndrome work, and reduce his Alzheimer's disease research. "We are having to drop our Alzheimer's work in an era where we should be picking it up", he says. "People are just going to leave this field", laments Nobel Prize winner Stanley Prusiner (Director of the Institute for Neurodegenerative Diseases, University of California, San Francisco, CA, USA), who says his own Alzheimer's disease research is suffering. "I'm trying to make up some of the deficits with private funding, but it is not sufficient...It's really hard right now."

Other researchers are making a more subtle research shift. Karen Duff (Columbia University Medical Center, New York, NY, USA) has opted to work in the area of neurofibrillary tangles, which occur in a number of neurodegenerative diseases, not just Alzheimer's disease. Importantly, this means that she can now get funding from the National Institute of Neurological Disorders and Stroke (NINDS). "I put all my grants through NINDS now", she says. "The decision to work exclusively on tangles is partly due to the lack of funding at NIA."

If researchers have a better chance of being funded by other NIH institutes, such as the NINDS, why has the NIA's funding line fallen so far? According

to an open letter to the research community from NIA Director, Richard Hodes, "[the] NIA has recently seen a rise in the number and average cost of applications submitted—the surge in applications has put additional pressure on our success rate and funding line". The letter also says that, as the research field has matured, applications have improved, leading to greater numbers being eligible for funding—ie, the competition is tougher—and that there has been increasing demand for clinical trial funding, which although exciting is also expensive. Furthermore, budgets across the entire NIH have not been rising in line with inflation.

Many researchers are sceptical, however. "The perception is that the NIA is suffering from a shortage of money not because a lot of researchers looked for funding from them, but because of how they allocated their resources", says Duff. "Most of the criticisms of NIA's funding policy revolve around their past funding of large grants such as programmes, centres, and in particular clinical trials that were often poorly justified scientifically", she says. Landreth adds that "the NIA adopted this translational medicine model in a very vigorous way. They put huge amounts of resources into clinical trials, biomarker studies, and diagnostic studies. The consequence of this is that basic science is their very last priority." And Ginsberg agrees: "The NIA put all their eggs in one basket in these enormous grants—they basically aced-out the little guy. Yes, revenues are down. Yes, there's not as much money as we all want, we recognise that, but it should be distributed in a fair and balanced, meritorious way."

Suggestions of "squandering" and "mismanagement" are unfair,

says Ronald Petersen (Director of the Alzheimer's Disease Research Center, Mayo Clinic, Rochester, MN, USA), who, since September, has been heading a National Advisory Council on Aging (NACA) committee established to review the NIA's extramural spending programme. "It might be perceived that way because NIA is doing large science now where it may not have 15 years ago, but I think that is a positive sign, reflecting maturation of the field rather than misjudgment on the part of the administration—20 years ago the aging institute [NIA] probably couldn't fund clinical trials because there was nothing to test."

Barr adds that "we [the NIA] do continue to support a robust portfolio of basic research. Could it be larger? Yes. But so could NIA's entire portfolio and we are trying to balance diverse research approaches across a broad mandate in a very tight funding environment."

Whether investment in big science is just a compounding problem or the cause for the NIA's current financial strife, Petersen warns that the NIA is unlikely to be an aberrant institute, and that other NIH institutes could well be heading towards single digit paylines. "Members of the committee have said the NIA might be the canary in the coal mine", he says. Indeed, several institutes, including the National Institute of Allergy and Infectious Diseases and the National Institute of Arthritis and Musculoskeletal and Skin Diseases, that have now announced their 2011 paylines reveal them to be similar to the NIA's.

Petersen's committee is gathering information and will most likely announce its conclusions and proposals for improvement to the NIA in May this year. In the meantime, Barr says that "the leadership at NIA empathises with the dilemma facing so many researchers", and that the NIA is "stretching every dollar" to try and improve the situation. They are reducing the dollar amounts of their awards by roughly 18%. They are also putting a cap on the total number of large grants

(those more than US\$500 000) that the institute will accept. With these and other measures, he says, "we expect to be able to make a 9% payroll in 2011 for grants under \$500 000".

Barr knows that even 9% is far from ideal, but explains that the 2011 budget for the NIH as a whole has not yet been determined. President Obama's administration proposed a cut of 0.3%, but the largely Republican House of Representatives rejected this and has instead called for a 5%, or \$1.6 billion, cut. Until the budget is settled, it is unclear how badly the NIH will be affected and whether the NIA will stand any hope of going beyond its 9% estimate.

At apparent odds with the threat of government spending cuts, in December last year, the US congress passed the National Alzheimer's Project Act, a plan to coordinate research efforts and combat the growing Alzheimer's disease crisis. According to figures from the Alzheimer's Association, by 2050, more than 13.5 million Americans are predicted to be affected by Alzheimer's disease, with the cost to government-run Medicaid and Medicare estimated at \$800 billion. The passing of the National Alzheimer's Project Act reflects the political recognition that investing in research for a cure is a top priority.

However, as Prusiner points out, the politicians are paying merely lip-service to the issue. "There's no money behind it—political gestures don't pay for post docs, professors, technicians. They don't pay for pipette tips, robots, chemicals. They do nothing."

In Europe, by contrast, funding of Alzheimer's disease and dementia research has taken an upswing. In France, for example, President Nicolas Sarkozy recently announced a €1.6 billion, 5-year National Plan for Alzheimer's disease to fund scientific efforts. And in the UK, the launch of the National Dementia Strategy for England has been gilded with a promise by the National Institute for Health Research that dementia research grants will receive priority



National Institutes of Health (NIH)

funding. "At the moment, the funding situation in the UK is looking more encouraging", says Clive Ballard (King's College London, UK). "Other countries are leading the way", worries Petersen, "and the United States is falling behind."

How might the dichotomy between political ideal and economic reality start to be aligned? Petersen suggests that, "at the top level of NIH, maybe even Congress, someone needs to take the situation by the horns and look at the allocations of the individual NIH institutes—I think the budget for the NIA should be increased, perhaps disproportionately to other institutes, because Alzheimer's and ageing are the health crises of the immediate future".

Few, if any, Alzheimer's researchers would disagree that extra funding for the NIA would help, but Landreth cautions that, "more money isn't going to do anything if it is spent the same way". Ginsberg adds: "the Director of the NIA Division of Neuroscience recently retired. Such leadership changes at the NIA are favourable, as fresh faces might be responsive to the broad spectrum of scientists who apply for funding." Thus, it seems that the NIA not only has a struggle on its hands to find funds, but also to restore the faith of the Alzheimer's research community.

Ruth Williams

For the Alzheimer's Association report please see <http://www.alz.org/index.asp>