

**Questions for NIH from Chairman Steve Buyer  
Subcommittee on Oversight and Investigations  
Committee on Veterans Affairs**

April 29, 2004

Hearing on VA Research on Alzheimer's Disease,  
Parkinson's Disease, and Diabetes

Question:

What are the top ten priorities in research at the National Institute on Aging (NIA)?

Answer:

The National Institute on Aging's core mission encompasses the following overall research priority areas for its extramural grant program:

- Alzheimer's disease and the neuroscience of aging
- Age-related diseases
- Biology of aging
- Behavioral and social aspects of growing older

The following six specific research areas are the complementary priorities of the intramural research program:

- **Molecular and Cellular Biology:** *caloric restriction, cell cycle control, signal transduction, DNA repair, physiology, medicinal chemistry, gene regulation, immunosenescence, vascular biology*
- **Neuroscience:** *neurodegenerative diseases, drug design and development; neuronal cell biology*
- **Genetics:** *genetic determinants of aging, cancer genetics, image informatics, computational biology*
- **Behavioral Research:** *personality, cognition, and psychophysiology*
- **Clinical Research** *Cardiology, Oncology, Immunology, Neurology, Endocrinology*
- **Epidemiology:** *frailty, cognition, body composition, disability, molecular biomarkers of aging*

Question:

On page 24 of the NIA's 2001-2002 AD Progress Report, it talks about a 5 year Indiana University Medical School research team that followed 2,147 African-Americans in Indianapolis and 2,459 Yoruba in Ibadan, Nigeria, to see whether they developed dementia and AD. All the study participants were 65 and older. Two-thirds were female. All participants at both sites received the same examination, which included a structured interview, neuropsychological testing and a physical examination. Results indicated that in the US group, 3.24 percent per year developed dementia, including 2.52 percent per year who developed AD. In the Nigerian group, 1.35 percent per year developed dementia, including 1.15 per year who developed AD.

What do these findings tell us? Are the differences significant enough to warrant further study of these two populations?

I noted that a second phase of the study is planned using the same populations, which will focus on genetic factors and non-genetic factors, including cholesterol levels, body mass index, hypertension, and diabetes. When will this study begin?

Answer:

The Indianapolis-Ibadan Dementia Project demonstrated that the incidence rates for Alzheimer's disease and dementia are significantly lower in the Yoruba population in Ibadan, Nigeria than in African Americans. The second phase of the study has been funded after favorable scientific peer-review and has already begun. Completion is projected for December 2005.

The risk for AD in Americans is now known to increase dramatically with age with nearly half of all individuals over age 85 thought to be affected.<sup>1</sup> By comparing populations with similar AD genotypes, the Indianapolis-Ibadan Dementia Project may further contribute to our understanding of potentially modifiable non-genetic factors to help slow or prevent the alarming trend in AD incidence. A detailed description is provided in the attached study abstract.

<sup>1</sup> Data from the Alzheimer's Association. See also Ernst, RL; Hay, JW. "The U.S. Economic and Social Costs of Alzheimer's Disease Revisited." *American Journal of Public Health* 1994; 84(8): 1261 – 1264. This study cites figures based on 1991 data, which were updated in the journal's press release to 1994 figures.

**Abstract: DESCRIPTION** (Adapted from the Applicant's Abstract): In the new application of the Indianapolis Ibadan Dementia Project, we are proposing to study intensively the risk factors which may explain the differences in incidence rates. As these risk factors are likely to be multiple, complex, involving genetic, environmental as well as genetic-environmental interactive influences, larger cohorts than those we currently possess will be required. We propose to enrich our current surviving cohort of 800 subjects in each site by recruiting an additional 2000 African Americans and 2000 Yoruba, 70 years and over, for a total of 2800 subjects at each site. With this enlarged sample we propose to measure ApoE genotypes and ApoE promoter haplotypes on all subjects in both cohorts. As exploration of site differences suggest that factors associated with increased vascular risk may be a productive line of investigation, we will also measure a number of biochemical values known to be associated with cardiovascular risk. We will continue to collect our current clinical, neuropsychological and socio-demographic data. With these new data we propose to test the following hypotheses. 1) Possession of the e4 allele of ApoE will be a stronger risk factor for AD in African Americans than in the Yoruba. The ApoE 2 allele will be protective for AD in the African Americans but not in the Yoruba. 2) Vascular risk factors increase the risk of dementia, AD and cognitive decline within each population site. The lower prevalence of these factors accounts for some of the differences in rates of AD and dementia between sites. 3) The interaction between ApoE genotypes and vascular risk factors alter the strength of the association between the ApoE 4 and 2 alleles and AD and account for some of the variation in AD rates between the populations. Our secondary aims are, 1) to continue to develop measurements of social engagement and activity levels which can be applied validly across sites; 2) to continue to evaluate natural history of cognitive and social functioning in two community-dwelling cohorts and to identify factors which may predict decline in cognitive and social function; 3) to determine if ApoE promoter haplotype is a risk factor for AD and correlate this risk with promoter transcriptional activity; and 4) to store blood, plasma and DNA samples for future genetic and biological studies.