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Aging Research: Collaborations Forge a Promising Future

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Abstract

The National Institute on Aging (NIA) is one of 27 institutes and centers at the National Institutes of Health (NIH), founded in 1974 to conduct and support research on aging and the health and well-being of older people. The Institute's interests span the fundamental processes that contribute to aging and their impact on systems, to diseases and conditions for which aging is a risk factor, to interventions that may prevent, delay, or treat these conditions and/or otherwise contribute to an extension of healthy, active years of life. NIA's growth over the past 40 years as well as its current areas of ongoing research have been marked by multiple fruitful research collaborations both within and outside the Federal government, spanning the breadth of the Institute's research activities. Several highlights of these collaborations, including the Health and Retirement Study, geroscience research, falls injury prevention in the elderly, and implementation of the National Plan to Address Alzheimer's Disease, are discussed from the perspective of past accomplishments and trends for the future.

Keywords

Research; Funding; Collaborations

While supporting research on aging was a laudable goal in the 1970s, it is an imperative now. The growth of the older population of the United States is impressive: from about 46 million persons in 2014, the population aged 65 and over will likely almost double by mid-century, and the population aged 85 and over is increasing at an even faster rate¹. While the increase in life expectancy at older ages was accompanied by a decrease in the prevalence of disability in the last decades of the previous century, there are signs that the favorable trend

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in disability at older ages has stopped and even has begun to reverse in recent years, especially for American women².

In anticipation of the accelerated aging of the U.S. population, the National Institute on Aging (NIA), currently one of 27 institutes and centers (ICs) at the National Institutes of Health (NIH), was founded in 1974 to conduct and support research on aging and the health and well-being of older people. The Institute plays a significant role in leading or supporting research on aging, and its interests span the fundamental processes that contribute to aging and their impact on systems, to diseases and conditions for which aging is a risk factor, to interventions that may prevent, delay, or treat these conditions and/or otherwise contribute to an extension of healthy, active years of life.

Collaborations have been key to the successful advancement of biomedical science and in the context of four decades of NIA-funded aging research, to understanding the issues that affect health and function at older ages. The NIH and NIA promote and model collaborative science, and have fostered a wide range of trans-agency programs and initiatives, as well as significant public-private partnerships, in the recent past – examples of which are discussed below. These collaborations have been enhanced by the level of visibility that aging research has attained in today's environment. And the products of these research collaborations, when used by individuals, clinicians, and policymakers to foster improvements in practice, should yield tangible additional benefits across all sectors of our culture, including the workforce, transportation, housing, and perhaps most critically – healthcare.

NIA's investment in its research portfolio has approximately doubled in the past eleven years, from a budget of just over \$1 billion in Fiscal Year (FY) 2006 to just over \$2 billion in FY2017. And what has this funding made possible? It's widely recognized that the NIA is the lead institute at the NIH for Alzheimer's and related dementias (AD/ADRD) research – and we have made tremendous strides in this area of investigation, from the discovery of additional risk genes for AD, the development of interventions that can help caregivers experience less stress, and advances in imaging that are enabling testing of very early interventions in individuals at high risk for AD, to the crafting of a complex infrastructure – in collaboration with NIH overall – that will enable acceleration of current and future exploration of new clinical targets. Many of these advances have occurred as the result of collaborations across NIH and beyond. As the NIA moves forward, collaborations to leverage the research investments by the institute will become even more critical, as the science becomes more complex, and resources required to answer complex questions are best leveraged by collaboration with other scientific groups.

In a previous commentary in the *Journal of the American Geriatrics Society*, NIA authors discussed the growth of the Institute's research portfolio as well as several of its flagship programs, such as the Baltimore Longitudinal Study on Aging and the Interventions Testing Program³. In this article, we revisit one of these programs – the Health and Retirement Study – and explore three other NIA priorities: geroscience research, falls injury prevention in the elderly, and implementation of the National Plan to Address Alzheimer's Disease. A key feature of each of these activities is collaboration – across the NIH, the Federal government, and non-governmental organizations.

Geroscience Research

The concept of “geroscience” was developed at NIH through NIA leadership to merge interests of basic aging and disease-focused researchers. It is inherently a field of collaborative work. While the public’s interest in a “fountain of youth” may grow as its average age increases, the NIA is not satisfied with increasing lifespan if this involves increased years encumbered by myriad health conditions that lead to disability and diminish quality of life. A primary goal of the NIA is increasing “healthspan,” which focuses on extending a person’s healthy and productive years. It is believed by many in the research community – as well as the NIA – that slowing the rate of aging may have a central impact on both the age of onset, and the severity, of these deleterious conditions. Geroscience is an emerging interdisciplinary scientific field that aims to understand the relationship between aging and age-related diseases/dysfunctions, and how these intersect with frailty and resilience. Researchers in the field hypothesize that slowing the rate of aging will have a beneficial impact on the health of older adults by delaying the onset or reducing the severity of most chronic diseases and frailty; i.e., improving healthspan.

The NIA has led the expansion of the geroscience field by launching several key collaborations. In 2012, the NIA launched a GeroScience Interest Group (GSIG)⁴, to bring together NIH ICs with an interest in research on the mechanisms noted above for their potential broad impact on the onset and progression of diseases of aging. Twenty-one of the 27 NIH ICs now participate in this interest group, providing both intellectual and financial capital to address the highest priority problems in the field. Recently, research has been funded in response to two separate Funding Opportunity Announcements emanating from the GSIG that demonstrate collaborative efforts among NIH institutes (Table 1).

The NIA also has led the development of two large summit meetings focused on geroscience, in collaboration with several non-governmental entities. In the fall of 2013, the NIH held (in collaboration with the Alliance for Aging Research and the Gerontological Society of America (GSA), the first ever Geroscience Summit, entitled *Advances in Geroscience: Impact on Healthspan and Chronic Disease*. The goal of this initial conference was twofold: 1) to generate a new vision of collaborative interactions that will advance understanding of how the molecular, cellular and systemic processes of aging affect the etiology of chronic diseases; and 2) to identify strategic scientific areas of overlap among divergent chronic diseases and suggest new research interactions or directions to address those areas that will promote health. Two publications on the importance and overarching impact of geroscience emerged from this meeting^{5,6}.

Based on the overwhelmingly positive response to the first summit, the NIH in the spring of 2016 again supported (in collaboration with the New York Academy of Sciences, the American Federation for Aging Research, and the GSA) a second meeting entitled: *Disease Drivers of Aging: 2016 Advances in Geroscience*. The goal of this second summit was to explore “reverse geroscience”: the impact of chronic diseases and their treatment on the rate of aging. Like the first summit, the meeting brought together a wide spectrum of researchers, representatives from pharmaceutical companies, government agencies, and non-profit organizations, who work in the fields of aging-related diseases (i.e., HIV/AIDS, cancer,

diabetes) and/or in aging research, to understand the impact of these conditions on aging. Both summits resulted in meeting publications that have expanded conversations around this emerging field of research (see above, and references 7 and 8, following the second summit). In addition, recognizing the potential importance of this sort of research to clinical care and disease management, the American Geriatrics Society and the GSA, two of the major organizations involved in aging and geriatrics in the U.S.A., have recently developed formal Geroscience Interest Groups.

Strategies to Reduce Injuries and Develop Confidence in Elders

Geriatricians and other healthcare providers appreciate that one of the greatest risks to seniors is that of falling, and recognize that a team effort is needed to prevent falls⁹. Nearly 30 percent of adults aged 65 years and older experience a fall each year, and falls are the leading cause of injuries (including those that are fatal) in this age group¹⁰. The causes of this increased risk are multifactorial, and include limitations in mobility and balance, as well as susceptibility to environmental hazards, among others. NIA-funded research in the past has supported the testing of multiple strategies that can reduce these risks^{11,12,13,14,15,16,17,18}, but how can the most successful of these findings be applied to a geographically and ethnically diverse community of older adults?

To address this critically important public health challenge, the NIA developed a Falls Injuries Prevention Partnership with the Patient-Centered Outcomes Research Institute (PCORI) in 2013. The product of this partnership thus far was the release of a Request for Applications for a randomized clinical trial of multifactorial, evidence-based, patient-centered strategy for preventing serious fall-related injuries among non-institutionalized older people. The NIA awarded funding for the Strategies To Reduce Injuries and Develop Confidence in Elders (STRIDE) trial – managed by investigators at Harvard, Yale, and the University of California at Los Angeles – in 2014. The focus of STRIDE has been to test an individually tailored prevention strategy and concept of a fall care manager in various health care systems and communities – in order to reduce serious fall-related injuries in individuals at or over the age of 75. Individual prevention strategies will be based on personal assessments for falls risks, and control participants will receive current standard of care treatment.

This study is unique in its level of stakeholder engagement, one of the goals of the PCORI collaboration. In addition to the universities listed above, investigators from NIA-funded Claude D. Pepper Older Americans Independence Centers, practitioners from 10 healthcare delivery systems and 86 primary care practice sites, along with participant representatives are all participating in the trial, which is expected to be completed in 2019. The participant representatives have been critical in bringing their own perspectives to the trial, in terms of issues like intervention adherence and their hopes regarding outcomes.

The Health and Retirement Study

The Health and Retirement Study is a prime example of a research infrastructure supported by NIA which facilitates a broad range of collaborations. Much of what researchers and

The National Plan to Address Alzheimer's Disease

Work to advance understanding and potential treatment of AD/ADRD is a powerful example of leverage of collaborations to advance the science. Research on AD/ADRD has entered an era of unprecedented excitement and scientific opportunity with the signing of the National Alzheimer's Project Act by President Obama in January 2011. This launched a series of events, including the establishment of a National Advisory Council for Alzheimer's Research, Care, and Services later that same year and the development of a National Plan to Address Alzheimer's Disease in 2012. Because the areas of focus of the National Plan go well beyond biomedical research, the Advisory Council includes membership from multiple Federal agencies (Table 2), as well as other public and private sector organizations.

Concomitant with this increased Federal attention to the spectrum of needs resulting from these devastating conditions, increased funding was also made available, including additional NIH allocations in FYs 2012 and 2013, and enhanced Congressional appropriations in FYs 2014-2017. Over this period, NIA/NIH received an \$875 million increase in AD/ADRD funding, with much of that increase occurring in the FY2016 and FY2017 appropriations (\$350 and \$400 million, respectively).

The increase in AD/ADRD funding in the last several years has called for enhanced collaboration of NIA with multiple institutes across NIH – particularly the National Institute of Neurological Disorders and Stroke (NINDS; see below), NHGRI (e.g., the Alzheimer's Disease Sequencing Project), and NICHD (e.g., the Down Syndrome Consortium, along with several other NIH ICs). To manage these increases in funds and to ensure that the AD/ADRD research community is poised to take advantage of any future funds provided, the NIA and NINDS issued a number of targeted FOAs in 2015 and 2016, to encourage proposals over a broad range of topics, including basic biology, translational and clinical trials, health disparities, and the challenges of caregiving (<http://www.nia.nih.gov/AD-FOAs>). Importantly, the topics in these FOAs span all of the NIA's research divisions – the Division of Geriatrics and Clinical Gerontology, the Division of Behavioral and Social Research, the Division of Aging Biology, and the Division of Neuroscience – and researchers from many subdisciplines of geriatrics will be needed to solve the problems outlined in the announcements. The response from the research community has been impressive, however innovative ideas from all corners of the aging research community are still needed to keep driving these fields ahead.

With respect to internal and external collaborations, the field of AD/ADRD research has been progressive. Twenty-two ICs already engage in AD/ADRD research (as of FY2016), and impressive examples of external partnerships are also in place and are marked by unprecedented openness and data sharing. The Accelerating Medicines Partnership and the Alzheimer's Disease Neuroimaging Initiative are both flagship examples of successful public-private partnerships that have and continue to accelerate research in Alzheimer's.

Aging Research across the NIH

These highlights showcase some key examples of NIA's investments in and collaborations on aging research. However, as the profile of this research area has grown, so has the interest among other ICs at the NIH. As of FY2016, the last year for which we have complete information, 24 NIH ICs and the NIH Office of the Director are investing in aging research at a level of just over \$3 billion. This research spans a wide array of research areas, including the basic science of aging organ systems; aging-related diseases/conditions such as cancer, glaucoma, and hearing loss; the impact of aging on the management of other health conditions, such as HIV; and research on intervening to improve these conditions and to support those caregivers helping loved ones experiencing them.

Conclusions

NIH has come a long way in supporting basic, translational, and clinical research on aging since 1974. As a result, we have greater insights into aging and are making significant and clinically meaningful strides in addressing the many conditions that contribute to morbidity and premature mortality in older people. However, much more remains to be learned about the biology of these conditions and which interventions may be the most impactful. We must have engagement and collaboration across scientific disciplines to make this happen, and we encourage the readership of the *Journal of the American Geriatrics Society* to join us in this effort.

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Table 1

NIH Institutes and Centers Participating in the GeroScience Interest Group (GSIG)

CSR	Center for Scientific Review
NCCIH	National Center for Complementary and Integrative Health
NCI	National Cancer Institute
NEI	National Eye Institute
NHGRI	National Human Genome Research Institute
NHLBI	National Heart, Lung and Blood Institute
NIA	National Institute on Aging
NIAAA	National Institute of Alcohol Abuse and Alcoholism
NIAID	National Institute of Allergies and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB	National Institute of Biomedical Imaging and Bioengineering
NICHD	National Institute of Child Health and Development
NIDA	National Institute on Drug Abuse
NIDCR	National Institute of Dental and Craniofacial Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIMH	National Institute of Mental Health
NINDS	National Institute of Neurological Disorders and Stroke
NINR	National Institute of Nursing Research
OD-NIH	Office of the Director - National Institutes of Health

Two recent Funding Opportunity Announcements showcase GSIG collaborations across the NIH:

PAR-13-233, *Chronic Inflammation and Age-related Disease*—funded by:

- National Institute on Aging
- National Heart, Lung, and Blood Institute
- National Institute of Environmental Health Sciences

RFA-AG-16-020, *Impact of Aging on Currently Employed Animal Models of Disease and Chronic Conditions: Demonstration Projects*—funded by:

- National Institute on Aging
- National Institute of Allergy and Infectious Diseases
- National Cancer Institute
- National Institute of Environmental Health Sciences
- National Institute of Neurological Disorders and Stroke

Table 2**Federal Members of the Advisory Council on Alzheimer's Research, Care and Services**

Department of Health and Human Services
• Office of the Assistant Secretary for Planning and Evaluation
• Administration on Aging/Administration for Community Living
• Agency for Healthcare Research and Quality
• Centers for Disease Control and Prevention
• Centers for Medicare and Medicaid Services
• Health Resources and Services Administration
• Indian Health Service
• National Institute on Aging/National
Institutes of Health
Department of Defense
Department of Veterans Affairs
National Science Foundation