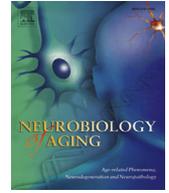




Contents lists available at ScienceDirect

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging

The expectation breakers

Molly V. Wagster^{a,*}, Jonathan W. King^b^a Division of Neuroscience, The National Institute on Aging, Bethesda, MD, USA^b Division of Behavioral and Social Research, The National Institute on Aging, Bethesda, MD, USA

ARTICLE INFO

Article history:

Received 17 April 2019

Received in revised form 21 April 2019

Accepted 22 April 2019

Ageism is alive and well in the hearts, minds, muscles, skin, eyes, and ears of the U.S. citizenry. We harbor the expectation that aging brings loss of all kind and dimension. The last several years have brought a new energy and focus to the goal of understanding, treating, and one day preventing Alzheimer's disease, perhaps the most dreaded malady of aging because it causes the progressive loss of memory, mental capacity, and eventually the self. Our best projections of future prevalence indicate that most of us will face this disease in some very personal way. However, many of us will thrive as we grow older and some will demonstrate superior cognitive performance for their chronological age. What characterizes these individuals who shatter our negative expectations? How can we unlock their secrets and share the code for optimal brain function?

Fifty years ago, [Blessed et al. \(1968\)](#) observed that the brains of some older adults without any cognitive impairment at death nonetheless had high enough mean amyloid burden to be indistinguishable from the brains of those who died with dementia, causing them to propose that these individuals demonstrate a "reserve capacity." These counterintuitive findings, as well as others from clinical studies of stroke, traumatic brain injury, or other insults, have led to the conceptualization of brain reserve, cognitive reserve, and resilience or resistance to neurodegenerative disease processes, neural damage, or age-related decline in brain function.

In 2017, the Foundation for the National Institutes of Health facilitated the continued partnership between the National Institute on Aging and the McKnight Brain Research Foundation to

sponsor the third Cognitive Aging Summit. The focus of the Summit was resilience and reserve; over 300 speakers and attendees convened to discuss the latest findings in the field. An executive session was held on the final day of the conference to discuss recommendations for ways to further advance the study of cognitive aging in the context of resilience and reserve, including (1) promotion of theories surrounding these concepts, coupled with the development of common scientific nomenclature and precise terminology; (2) encouragement of new large-scale longitudinal studies in humans who that employ multimodal neuroimaging and other biomarker assessments; (3) facilitation of the aggregation and comparison of data across existing studies to seed the field more quickly with information on key factors and novel therapeutic targets; (4) characterization of the epigenome of the aging brain; (5) initiation of longitudinal studies of neuroadaptive processes over the lifespan in shorter-lived animal models; and (6) development of registries and data sets for the study of optimally healthy cognitive aging, the so-called cognitive "super agers."

This Special Issue of *Neurobiology of Aging* highlights the major themes and specific research findings presented at the Summit. The sessions were organized around a set of key questions. Session 1, *How Do We Operationalize Brain Reserve, Cognitive Reserve, Cognitive Resilience, and Compensation?*, was devoted to issues related to definitions for and measurement of brain reserve, cognitive reserve, and related concepts. Session 2, *What Are the Threats to Successful Brain and Cognitive Aging?*, explored ways in which the structure and function of the brain changes over the lifespan. Session 3, *What Are the Earlier Life Contributions to Reserve and Resilience?*, highlighted the state of our knowledge into the ways that the anatomy, physiology, and function of the brain arise from a combination of both developmental processes and environmental influences. Session 4, *What Are the Later Life Contributions to Reserve, Resilience, and Compensation?*, complemented the previous session by delving into the later life experiences and lifestyle choices that contribute to the

Disclaimer: The participation of these individuals or the materials should not be interpreted as representing the official viewpoint of the U.S. Department of Health and Human Services, the National Institutes of Health, or the National Institute on Aging, except where noted.

* Corresponding author at: Division of Neuroscience, The National Institute on Aging, Gateway Building, Suite 3E400, 7201 Wisconsin Avenue, Bethesda, MD 20892, USA. Tel.: 301-496-9350; fax: 301-496-1494.

E-mail address: wagsterm@nia.nih.gov (M.V. Wagster).

brain's ability to protect against, respond to, and compensate for pathological insults. Session 5, *How Do We Validate Approaches that Aim to Harness Reserve to Improve the Aging Brain?*, addressed the development of accurate and reproducible ways to quantify reserve, compensation, and resilience in aging individuals. Finally, Session 6, *Innovative Approaches in Cognitive Aging*, explored novel approaches and models to address cognitive aging and to delay or prevent cognitive decline in older individuals.

Fueled by this increase in our collective knowledge, and with specific plans for future activities, we hope to accelerate our research investment to determine the combination of genetic/epigenetic, lifestyle, social, and personality factors that lead to the maintenance of function and what factors do not play this role. Healthy brain and cognitive aging continue mainly to be explored secondarily to, or in contrast with, impairment and disease. A fresh

perspective to understand neuroadaptive processes with age and the elements that drive maintenance of healthy neural and behavioral function will lay the foundation and provide the opportunity for us all to be expectation breakers.

Disclosure

No disclosures.

Reference

Blessed, G., Tomlinson, B.E., Roth, M., 1968. The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *Br. J. Psychiatry* 114, 797–811.