Clinical, Imaging, and Pathological Studies in the Oldest Old: The 90+ Study

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Country

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Clinical, Imaging, and Pathological Studies in the Oldest Old: The 90+ Study

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Alzheimer's disease & other dementias

Keywords

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Research Abstract

DESCRIPTION (provided by applicant): People aged 90 and older (the oldest-old) comprise the fastest growing segment of the population and have the highest rates of dementia. Nonetheless, little is known about the causes of dementia in this age group. Approximately half of demented of oldest-old individuals do not appear to have significant pathology to explain cognitive loss, while a similar proportion of non-demented oldest-old have high levels of Alzheimer's disease (AD) and other pathologies while maintaining good cognition. Moreover, risk factors are largely unknown in this age group and appear paradoxical, with traditional risk factors such as hypertension appearing to be protective for dementia. The primary goal of our proposal is a better understanding of the risk factors and biological substrates for the expression of dementia in the oldest-old. Focusing our studies on the clinical pathological discordance for dementia and the paucity of knowledge of risk factors in this age group, we hypothesize that AD, vascular, and other pathologies represent preclinical disease in non-demented oldest-old (significant pathology without dementia) and thus will be associated with greater rates of cognitive decline and dementia in prospective studies (Aim1). In contrast, individuals who have dementia without significant pathology will, in fact, have low levels of multiple pathologies that contribute additively to cognitive impairment (Aim 2). Because multiple dementing pathologies, not just AD, appear to contribute to cognitive loss in people with advanced age, we will investigate risk factors in relation to specific pathologies, identified on autopsy or imaging (Aim 3). Risk factor data collected in the Leisure World Cohort Study (1980s) and The 90+ Study (2003-present) will provide our investigations with a rich dataset spanning several decades, and can contribute to our understanding of the changing relationship of risk factors with age. In addition to traditional risk factors, such as APOE, exercise, and physical performance, we will study novel factors (fluctuations in blood pressure and O2 saturation). For these investigations, new procedures have been added to our epidemiological study, including neuroimaging (structural MRI and florbetapir amyloid PET) and ambulatory 24-hour monitoring of blood pressure (BP) and O2 saturation. We hypothesize that normal BP is a risk factor for dementia because daytime and nocturnal BP fluctuations lead to hypotension increasing the risk of microinfarcts and vascular cognitive impairment. Hypoxia in the oldest-old will be associated with increased amyloid deposition and AD related pathologies, as well as with microinfarcts, thereby increasing the risk of dementia. We anticipate more than 2/3 of our subjects will participate in The 90+ Autopsy Study, adding further value to our clinical, genetic, and imaging studies in these well characterized population-based subjects. On completion of The 90+ Study, we anticipate making all of our data publicly available for research (Aim 4). The 90+ Study will provide a wealth of information about the oldest-old, an important and growing segment of our population. The knowledge obtained from these investigations can have profound public health impact.

Lay Summary

PUBLIC HEALTH RELEVANCE: People over 90 (the Oldest Old) are the fastest growing segment of our population and have the highest rates of dementia, although causes and risk factors are largely unknown. With clinical, imaging and pathological investigations, the primary

goal of this proposal is to better understand the risk factors and biological substrates for dementia in a population-based sample of our oldest citizens. Information from these investigations has the potential for enormous public health impact in ameliorating the burden of dementia in our oldest citizens.

Further information available at:

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