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INTRODUCTION

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The Aging Brain

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According to the United States Department of Health and Human Services Administration on Aging, more than 14 percent of the US population is 65 or older, a percentage that is predicted to steadily increase over the next several decades. The rapid growth of this segment of the population is not a phenomenon limited to the United States — the global population is aging as well. A recent report by the Population Division of the United Nations Department of Economic and Social Affairs indicates the worldwide number of individuals ages 60 and older is set to double by 2050.

As this demographic shifts, certain medical challenges are anticipated to heavily affect the aging members of the world, as well as the caregivers and loved ones who help support them. This issue of the Yale Journal of Biology and Medicine (YJBM) addresses some of the largest concerns and challenges facing this expanding community of elderly individuals. The degeneration of the brain, loss of memory, compromised motor functions, loss of vision, slow injury recovery, and the effect of chronic substance abuse are issues that are essential to this community. Understanding the underlying biological mechanisms of physiological changes that occur in later stages of life is critical to diagnosing and treating age-related disease. This issue on The Aging Brain provides various insights into the means to more effectively treat and care for this valued segment of the population.

The Alzheimer's Association suggests that one in three senior citizens in the US will be affected by Alzheimer's disease (AD) and other forms of dementia. Although there is no cure for AD, scientific studies in the past decade have provided insight into the causes of neural damage and potential treatment approaches. To better clarify the current gaps in our knowledge surrounding the sequence of pathogenic events in AD and elucidate the current efforts and studies around these events, this issue begins with an interview with Dr. Christopher van Dyck, the Director of the Alzheimer's Disease Research Unit at the Yale School of Medicine. Dr. van Dyck discusses current neuroimaging studies working to understand disease pathogenesis *in vivo* and efforts to test new AD therapeutics in humans. Arbor, LaFontaine, and Cumbay discuss new information regarding amyloid beta structure and protein processing pathways, as well as obstacles hindering scientists from understanding the underlying causes of dementia and developing curative therapies. Tincer et al. describe the potential uses of neural stem cells and progenitor cells in treating AD, a method that holds great promise in reversing neural degeneration that occurs with the disease.

Another neurodegenerative disease primarily affecting the aging population is Parkinson's disease (PD). Patients with PD lose dopaminergic neurons in the *substantia nigra*, which causes problems with speech, movement, and balance. Borovac provides a clinically relevant review of the current dopamine agonists used as therapeutic agents to treat the symptoms of PD.

While some disorders primarily affect certain regions of the brain, it is also important to recognize the interconnectivity and effects that different systems in the brain can have on each other. Mohan et al. introduce the clinical significance of the brain's Default Mode Network and its role in various neurological and neuropsychiatric disorders, including AD. This article provides a unique perspective on how different regions of the brain interact and the effect these interactions have on the development and occurrence of symptoms.

O'Callaghan and Kenny explore the neural control of the cardiovascular system and the various links between neurocardiovascular instability and cognitive decline often seen in dementia. Co-occurrence of various neurocardiovascular symptoms and neurodegeneration as highlighted in this article is common, but has not been explicitly discussed in the literature. This review compiles evidence from many studies in a detailed description of the pathophysiology and emphasizes that,

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while a causative relationship is often not clear, the close association is important for clinicians to recognize.

Glaucoma, the leading cause of irreversible blindness in the world, is a disease with limited treatment options affecting many elderly individuals. Gauthier and Liu focus on the pathophysiology of glaucoma as well as more recent studies linking glaucoma to neurodegeneration beyond the eye and into the brain. The authors review the current treatment options for glaucoma, suggesting a new direction research should head in order to cure this widespread cause of blindness.

Neurodegenerative diseases are not the only significant medical situations that aging patients may encounter. This issue highlights several interesting articles exploring other aspects of the aging brain such as injury recovery, community health and social activities among the elderly, and perception of aging. Severe symptoms of neurodegenerative diseases, injuries, stroke, or surgery greatly affect the daily quality of life of elderly patients. Barss et al.'s review focuses on the topic of "cross-education," or the phenomenon that muscle training on one limb can improve the performance of that limb as well as the opposite, untrained limb. This idea has been around for a century, but only recently has it been viewed in terms of neural plasticity.

This issue also explores the external events that may affect the health of elderly individuals as they adjust to new limitations. Elderly patients will engage in discussions with caretakers and physicians about their ability to operate a vehicle safely. Isbel and Berry evaluate the effect that driving a car has on the connectedness and well-being of older people. These authors remind physicians evaluating the safety of elderly drivers to consider the role driving to events within the community has on the overall health of elderly patients. Additionally, the authors suggest further studies to ensure steps are taken to provide other means of transportation and participation in community activities when older people lose their capacity to drive.

In an effort to urge readers to better understand the aging process and ensure younger generations adequately care for our aging population, we close this issue with three outstanding pieces related to the perception of aging: Calamia et al. surveyed college students and community members in Louisiana to assess individual's knowledge of how memory and cognition change as we age. This study provides insight into factors affecting the perception of aging and suggests increased efforts to educate individuals of what constitutes normative versus pathological memory development. Further, the authors suggest additional research is needed to investigate how increased levels of understanding into the ways aging affects memory may influence public health outcomes.

One aspect of public health that affects individuals of all ages is addiction, a subject explored in YJBM's September 2015 focus issue. Expanding on this topic, De Jong et al. emphasize the increased need for training and education of medical students on substance-related disorders. The authors highlight the fact that alcohol use disorder is a growing problem in the geriatric population, and prescription drug misuse and nicotine addiction affect these older individuals, accentuating the need for addiction medicine training to address problems specific to this population.

Finally, we present an essay by Richard J. Franke, distinguished Yale alumnus, class of 1953, founder of the Franke Program in Science and the Humanities at Yale and supporter of the Yale Whitney Humanities Center. Franke's essay eloquently introduces the importance of narrative medicine in end-of-life care. He urges doctors to not only consider the medical wishes of a patient, but to ensure that the treatment prescribed is patient-centered and aligns with the values and characteristics that encapsulate the patient's life story. The author expounds on the implications of increased palliative care and its ability to lessen the emotional challenges associated with end-of-life care.

This issue reviews a wide scope of medical factors affecting the aging brain. Various authors offer unique perspectives of interactions between different brain regions to present a more cohesive understanding of abnormal neural networks and cognitive decline in the growing geriatric population. The articles presented specifically focus on increasing our understanding of the biological pathology affecting the aging brain and the external influences that may improve patients' quality of life.